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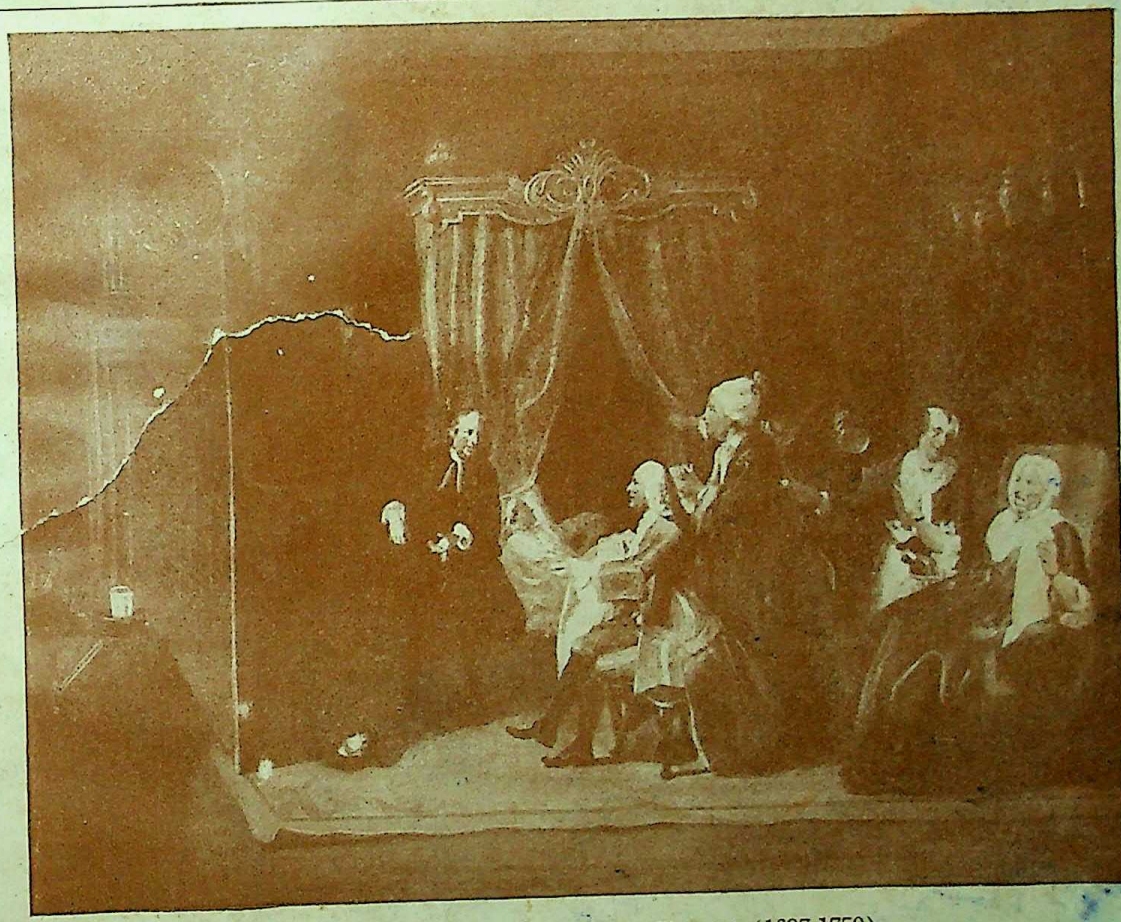
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The Journal of Organotherapy

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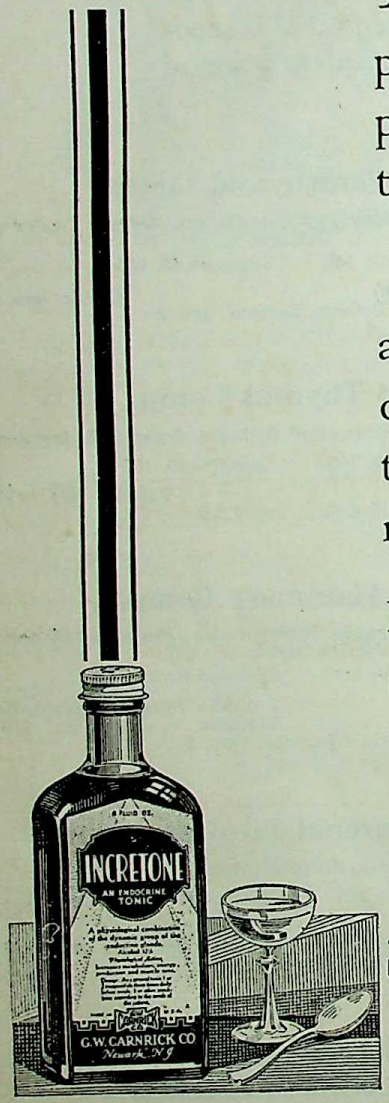
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The Action of Posterior Pituitary Preparations on the Intestine

POSTERIOR PITUITARY preparations contain a substance or substances that exert a specific action on the intestine. This action may be made use of clinically.

THE very earliest investigations of the pharmacological properties of extracts of the post pituitary lobe gave evidence of a diversity of actions — oxytocic, diuretic-antidiuretic, pressor, metabolic, etc. One of the effects of these solutions which subsequently came to be utilized in practice was the effect of stimulating contractions in the unstriped muscle of the bowel. Special preparations marked "surgical" to distinguish them from preparations for obstetrics were placed in the market for use in intestinal paralysis following abdominal operations, etc. Bell (*The Pituitary*) particularly endorsed the use of post pituitary in these conditions.

Without question this application must have been attended with a fair degree of success, yet it is interesting to note that even in the earliest reports there was evident a decided difference of opinion as to the effect of post pituitary on the intestine. The weight of evidence was in favor of an effect in stimulating contractions although reports of exactly opposite effects frequently appeared. Shamoff (1) reported:

"In view of the foregoing observations, it may be stated that there exists in the posterior lobe of the pituitary body some substance which has an action on the isolated intestinal loop resembling the action of adrenalin, a sub-

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stance moreover which may be other than that which raises blood pressure and causes diuresis. The substance is not constant in the extractives prepared in the usual ways and may indeed be inconstant in the fresh glands from which these substances are prepared. The most definite relaxations were obtained from 'Hypophysin' and from Armour's preparation made by drying the extract of the gland in vacuo at body temperature. Its presence or absence in the extracts may depend on the method of preparation and more accurate studies can only be made when this is perfected or when the active principle or principles of the gland become known and are capable of synthesis.

"As the matter stands, it may be concluded that certain posterior lobe preparations are capable of producing relaxation of the isolated intestinal loop and of inhibiting its rhythmic contractions, resembling in this respect the extracts of the adrenal medulla."

Numerous other observers reported depression of tonus and contractions and Hoskins (2) reported both depression of tonus and peristalsis in five out of six dogs injected intravenously with pituitrin. Many investigators cast doubt on the existence of a pituitary principle with a specific action in causing contractions in plain unstriped muscle. Others reported preliminary relaxation followed by subsequent increased tonus and contractions. One element of uncertainty in the several communications was a failure to take into account or report on such factors as added chemical compounds (chloretone, etc.), the pH of the solution and the existing state of tonus at the time of the experiment.

The contradictory character of these reports and reports of the same investigator of both increase and decrease of tonus and contractions made further investigation of the subject necessary. Gruber and Robinson (3) investigated the action of pituitary extracts on unanesthetized animals with a permanent Thiry-Vella fistula, noting the effect on intestinal contractions and tonus. Their work was done not only with post pituitary extracts but also with the separated elements vasopressin (the pressor principle) and oxytocin (the oxytocic principle). Their conclusions follow.

"1. Pituitary extract or pituitrin 'S' injected intravenously, intramuscularly or subcutaneously in unanesthetized dogs causes a decrease of tonus and decreased force of rhythmical contractions in the Thiry-Vella fistula of the ileum. After the temporary decrease in general tonus sudden changes in the tonus are observed which appear to be peristaltic movements. These simulate 'incomplete tetanus' of the intestine.

"2. The actions of 'Vasopressin' and of 'Oxytocin' are identically the same as that of pituitary extract.

"3. The changes in tonus of the intestine are probably not dependent upon the original state of tonus of the loop of intestine.

"4. The effects of pituitary extract, vasopressin and oxytocin are not due to the impurities choline and histamine.

"5. Histamine causes an increase in the tonus of the intestine of unanesthetized dogs.

"6. The decrease in tonus of the intestine following the intravenous injection of pituitary extract, vasopressin or oxytocin is independent of the changes in general arterial blood pressure."

Gaddum (4) reported results essentially similar, using strips of the colon, ileum and jejunum in the experiment. He also reports that particularly in the colon an inhibition usually preceded the stimulation.

"It was found that, though both preparations produced shortening of an isolated loop of the rabbit's intestine, and an increase in the peristalsis recorded by a modification of Trendelenburg's method (Garry, *Arch. exp. Path. u. Pharmakol.*, 120 : 348, 1927), vasopressin produced these effects in smaller doses than oxytocin. The effect is rather irregular and is apt to disappear after large doses, and sometimes spontaneously. The colon appeared to be more sensitive than the ileum, and the

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ileum than the jejunum. In the colon there was usually an inhibition before the stimulation. The effect on peristalsis was more regular than that on length of a segment, and was produced by smaller doses. The substance producing these effects was certainly not histamine, because quantities of histamine, hundreds of times larger than could possibly have been present, had no such effect: further, the active substance was destroyed by treatment with cold alkali. It was not the oxytocic principle, because, although the effects were produced by comparatively small doses of the international standard, a quantity of oxytocin containing twice as much of the oxytocic principle had no effect. On the other hand, this action may be due to the pressor principle. It was found that equipressor doses of the standard and of vasopressin produced similar effects on the bowel. It was not found possible to make a precise estimate of their relative potencies."

Gruber and Pipkin (5) using longitudinal excised segments of intestine, seem to have determined that the character of the effect (relaxation or contraction) induced by pituitary solutions depends upon the concentration of the preparation and the existing state of tonus. They say:

"1. High dilutions of pituitary extract if effective cause an increase in tonus and tonus oscillations in longitudinal segments of excised dog's intestine.

"2. High concentrations of pituitary extract cause an immediate loss in general tonus and complete disappearance of the rhythmic contractions.

"3. The degree of tonus normally present in the segment before the addition of pituitary extract is a factor in the results obtained. If the tonus is high, even dilute solutions may cause relaxation while if the tonus is low the strong solution may stimulate the gut.

"4. Morphine sulphate increases the tonus and, in many instances the height of rhythmic contractions, in excised segments of normal dog intestine. A similar action is noted in excised longitudinal segments taken from a Thiry-Vella loop.

(*Concluded on page 370*)

The Effect of Posterior Pituitary Preparations on the Blood Pressure

THE POSTERIOR PITUITARY BODY contains an active principle the predominant action of which is elevation of blood pressure and slowing of the heart. An unexplained depression of blood pressure preliminary to a sustained rise is usually noted.

THE rise in blood pressure, slowing of the heart and contraction of the blood vessels were among the first demonstrated effects of extracts of the pituitary body. Howell (1) showed that the principle causing this was limited to the posterior lobe. Dudley (2), Schlapp (3), and Draper (4) gave evidence that there are more than one active principle in the post pituitary and that the pressor and oxytocic principles are distinct, the diuretic-antidiuretic action apparently residing in the pressor substance. Later Kamm and his associates (5) demonstrated that a specific pressor principle can be isolated

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from the post pituitary. This is entirely distinct from the oxytocic principle but is apparently responsible for the diuretic-antidiuretic effects and in large part for the effect on smooth muscle (6). Kamm (5) found that:

"1. The posterior lobe of the pituitary gland contains two important active principles: one which raises the blood pressure and another which stimulates contraction of uterine muscle.

"2. A substantially complete separation of these two active principles has been accomplished by the employment of salting-out methods and, subsequently, by the use of appropriate solvents and precipitants.

"3. Solutions of these separated active principles have been recombined to form a pituitary extract identical with the original from which they were prepared, thus proving that no decomposition has taken place.

"4. The substantially pure pressor principle (β-hypophamine) has been obtained in the form of a white, stable, water-soluble powder 80 times as potent as the International Standard Powdered Pituitary.

"5. The separated oxytocic principle (α-hypophamine) has been obtained in the form of a white, stable, water-soluble powder which is more than 150 times as potent as the International Standard Powdered Pituitary.

"6. The pressor principle has been shown to be responsible for the diuretic-antidiuretic action of pituitary extracts.

"7. The pressor principle when tested on animals for demonstration of pressor effects shows the development of tolerance which is characteristic of active pituitary extracts. It has been shown to possess no appreciable depressor action.

"8. Both active principles are basic bodies, presumably amines."

The precise effect of pituitary upon blood pressure, however, has not been clearly established.

Most observers agree that there is a final large rise in tension, a slowing of the heart and a contraction of the blood vessels. Early observers reported that after a preliminary injection of pituitary, subsequent injection gave either no effect or even a reversal of effect—lowering of tension. Professor Abel, one of the earliest of all contributors to the subject reported results of this kind. Such effects have been ascribed to a hypothetical depressor substance while others have asserted that the subsequent fall in pressure is due to properties inherent in the pressor hormone itself. Kamm and his associates (5) have demonstrated that the pure pressor principle is free from this inversion effect.

"We have repeated the historical experiments of Howell (*J. Exp. Med.*, 3 : 245, 1898) and of Schafer and Vincent (*J. Physiol.*, 25 : 87, 1899) who have shown that when doses of pituitary extracts are administered intravenously in fairly rapid succession and in relatively large amounts a tolerance is quickly established so that after the second or third injection no further pressor effect is demonstrable.

"When plain pituitary extracts are used the typical rise in pressure may actually be replaced by a depressor action due either to the presence of traces of histamine or to the acidity. Abel (*J. Pharmacol. and Exp. Therap.*, 22 : 303, 1923) has demonstrated this depressor action even with his purified fraction.

"In repeating this early work we have used a purified pressor fraction and find that it acts exactly like an unmanipulated pituitary extract in respect to the development of tolerance, thus showing that the product has not been modified. However, the successive large doses fail to give any depressor action, thus attesting to the degree of purification of the product."

Stehle (7) also finds that "Preparations of the posterior lobe of the pituitary gland made as described show no reversal of action upon the blood pressure upon repeated injection at ten minute intervals."

Kamm does not believe the depressor action evident in posterior pituitary extracts to be

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either histamine or a special specific depressor principle, rather he believes it to be due to the oxytocic principle which he shows is extracted by pure ethyl alcohol.

"Schafer and Vincent (*loc. cit.*) not only demonstrated the presence of a depressor substance but showed that it is extractable from the glands by means of alcohol. Recent workers (for references see the excellent paper by Sharpey-Schafer and Macdonald, *Quart. J. Exp. Physiol.*, 16 : 251-280, 1926) have attached considerable significance to this depressor product, some referring to it as histamine.

"When acetone-desiccated glands are extracted with absolute ethyl alcohol in a Soxhlet extractor, this depressor product is readily removed. We have tested it by three methods, as is shown in the following table:

Assays Based on Extract from 1 G. of Desiccated Posterior Lobe

(a) Colorimetric assay for histamine	< 1 mg.
(b) Blood pressure assay for histamine	< 1 mg.
(c) Oxytocic assay	80 Oxytocic units = 100 mg. histamine

"According to the oxytocic assay, approximately 100 mg. of histamine is indicated as being extractable from 1 g. of gland material. The blood pressure assay, however, indicates the presence of even less than 1 per cent of this large quantity of histamine and the colorimetric test agrees in demonstrating that histamine is present only in small amounts. Two conclusions might be drawn: first, the depressor principle is not histamine but rather a substance much more potent than histamine in its oxytocic action: second, a small amount of histamine is present in the gland but in the process of alcohol extraction there is extracted simultaneously some of the true oxytocic principle.

"We believe that the second conclusion is correct. Since the oxytocic principle is soluble in alcohol, there is no reason why it should not be extracted and our results show that in six hours' extraction approximately 10 per cent of the oxytocic principle is removed."

It seems fairly certain that pure pressor principle displays little or no depressor action on subsequent injections although numerous observers describe a drop in pressure preliminary to a sustained rise. Gruber and Kountz (8) report results of this kind. They attribute to the preliminary fall in blood pressure a very important function in causing the subsequent sustained rise in pressure. They state:

"In the unanesthetized dog following the injection of pitressin the heart rate at first decreases during the primary rise in blood pressure, then it accelerates during the drop in blood pressure and decreases again during the secondary prolonged rise in blood pressure. Similar findings were recorded in dogs under either chloretone or ether anesthesia.....

"The acceleration in heart rate which occurs during the fall in blood pressure after the injection of pitressin is mainly if not wholly a reflex compensatory phenomenon. The sudden fall in blood pressure reflexly exciting the cardio accelerator center, is an attempt on the part of the cardio-vascular system to maintain a normal blood pressure.

"The slowed heart rate caused by the injection of pitressin is partly a reflex due to stimulation of the cardio-inhibitory center through the depressor nerve, and partly due to a direct action upon the heart muscle itself, the latter due probably to injury through vasoconstriction of the coronaries."

Stehle (*loc. cit.*) also notes a depression of pressure on first injection. "Tracing 2, which is not representative of the results as a whole, shows two blood pressure maxima on first injection and the fall between the rises is to a point below the pressure just prior to the injection. This is not to be regarded as a reversal of action since it occurs with the *first* injection and does not appear with later injections. What caused this effect is not clear but we hope to make the phenomenon the subject of further study."

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The initial depressor action of pituitary extracts is not yet fully explained. The existence of a specific depressor principle is not definitely excluded. The cardio-vascular compensatory mechanism may explain it without recourse to such a substance. A reversal effect on repeated injections seems to be disproved if pure pressor preparations are used. Apparently when the initial rise of pressure occurs the heart action slows; when the drop in pressure comes, the heart action increases and then during the prolonged characteristic rise of pressure the heart again slows up.

1. Howell, W. H., *J. Exp. Med.*, 3 : 245, 1898.
2. Dudley, H. W., *J. Pharmacol. and Exp. Therap.*, 14 : 285, 1920.
3. Schlapp, *Quart. J. Exp. Physiol.*, 15 : 327, 1925.
4. Draper, W. B., *Am. J. Physiol.*, 80 : 90, 1927.
5. Kamm, O., Aldrich, T. B., Grote, I. W., Rowe, L. W., and Bugbee, E. P., *J. Am. Chem. Soc.*, 50 : 573, Feb., 1928.
6. Hjort, A. M., *Endocrinology*, 12 : 496, 1928.
7. Stehle, R. L., *Am. J. Physiol.*, 88 : 724, 1929.
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Clinical Observations concerning Respiratory Basal Metabolism

(Translated from the article by Prof. F. de Quervain and Dr. F. Pedotti, First Assistant Physician at the Surgical Clinic, Berne.)

(*Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 39 : 646, 1926.)

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(Continued from Vol. XIV, No. 5)

II. General Relationship between Basal Metabolism, Pulse, Volume per Minute and Respiratory Quotient

In accordance with the survey of our experimental material we have concerned ourselves with the question of whether the elements concerned: Pulse, volume per minute and respiratory quotient, have a constant relation and whether this relation could accomplish anything for the determination of the basal metabolism for clinical purposes, and eventually for the thyroid gland. For the investigation of this problem we have made distribution tables of the individual relationships and we shall discuss the problem in the light of these tables. We have worked out the tables for the collective material as well as for the thyroid gland material alone, but we give the latter here again since only they are authoritative for the solution to the problem presented.

(*a*) *Relationship between Respiratory Quotient and Basal Metabolism*

We know from the respiratory quotient $\frac{\text{Vol. } CO_2}{\text{Vol. } O_2}$, that the higher it is the more carbohydrate is burned and the lower, the more fat is consumed. In cases of pure fat con-

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sumption it is 0.71, in pure carbohydrate consumption 1.0. If an individual who has fasted for 12 hours after a light meal shows a high basal metabolism, he can not proceed further at the cost of administered carbohydrate, but he must first of all resort to the body itself. Hence the respiratory quotient drops, and the lower it goes, the higher the basal metabolism and the more the body fat must be assailed. It is of interest to investigate how far this theoretical supposition is carried out in practice. In the accompanying distribution table

Table 4. Respiratory Quotient and Basal Metabolism

0

	−	−	−	−	+	+	+	+	+	+	+	+	+	+
R.Q.	30-39	20-29	10-19	0-9	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-x Basal Metabolism %
To 0.72			. . . . . .	. . . . . .	. . . .		. . . . .		.		.	.	.	.
0.73-0.75			. . .	. . . . . .	. . . .	. . . .	. . .	. .	. .	.			.	
0.76-0.78	.	.	. . . .	. . . .	. . . . . .	. .	. . . .	.	. . .	.		.		
0.79-0.81	.		. . .	. . . . .	. . . . .	. .		.		.				
0.82-0.84		. .	. . . .	. . . .	. . . . .			.						
0.85-0.87		.	. .	. .	.	.								
0.88-0.90		.	.	. . . .	. . . .									
0.91-0.93				. .	. .									
0.94-0.96					.									

0

the majority of values group themselves pretty well about the null line of basal metabolism and about the average value of respiratory quotient usually considered to be about 0.82. If the distribution of values be considered, there is a very evident interdependence, in that the further toward the plus calculation the basal metabolism goes the lower the respiratory quotient is. It is evident that in a larger amount of material this will be still more impressive. On the other hand we observed minus quantities of basal metabolism in the lowest respiratory quotients. The state of interdependence is only relative and we can not with any sort of certainty, draw conclusions from the amount of the respiratory quotient. The fact that very variable height of respiratory quotient is to be found even in basal metabolism values grouped about the null line is associated with the fact that in individual experiments, even with the same basal metabolism fat consumption extends to various levels, and that the body, despite the abundance of its last carbohydrate alimentation, and its level of glycogen content rapidly attacks its own fat in various manner.

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(b) *Relationship between Pulse Frequency and Basal Metabolism*

That a relationship must exist between pulse frequency and basal metabolism is shown in the comparison between the Basedow patients and the cretins. By a glance at the distribution table, No. 5, without further indication, one can see that the values run diagonally from the lowest pulse frequency and the lowest basal metabolism to the highest frequency and the highest basal metabolism. Likewise, it can be seen that the greatest number of findings are compactly grouped about

Table 5. Pulse Frequency and Basal Metabolism

Pulse	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-x Basal Metabolism %
40-49			1											
50-59		2	2	3	1									
60-69	1	1	6	7	4									
70-79		2	7	8	6	2								
80-89			1	6	8	5	3							
90-99	1			2	5	1	1	1						
100-109			1	2	3	2	3	3	1					
110-119					1		1	1	1		1	1		
120-129					1		3		4	2		1	1	1
130-139							1			1			1	

the pulse rates from 60 to 89 and about the basal metabolism value of ± 10 per cent. This relationship only holds good, however, for our material. A series of heart disease cases would give an entirely different picture, for in this case an increase in pulse frequency is not synonymous with the rise of the combustion process. Certain deviations are also found in thyroid gland cases, for here, too, factors unassociated with the thyroid gland are not rarely involved. The pulse frequency, then, permits us to draw a fairly good, but not absolute conclusion concerning the basal metabolism.

The relationship between pulse frequency and basal metabolism was the subject of another investigation. According to Means and Minot an increase of B. M. of around 50 per cent corresponds to an average rise of pulse frequency of about 65 per cent. The same numerical ratio was found by these authors for leukemia, in which instance, as is well known, a specific rise of B. M. was found. Our distribution tables approximately agreed with the findings of Means and Minot. The report of these authors is noteworthy, namely that in healthy people an increase of about 50

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per cent in metabolism during muscular work, implies an increase of only 25 per cent in pulse frequency.

Field and Back have very recently compared the volume of heart beat in M. Basedowii and in myxedema and found in the former an increase of about 16 per cent and in the latter a decrease of about 50 per cent.

(*c*) *Relationship between Volume per Minute and Basal Metabolism*

Without further explanation it is evident that the volume per minute is closely related to the basal metabolism, *i. e.*, in general a high value of volume per minute signifies a high rate of basal metabolism and *vice versa*. In the distribution table this fact is very prominent. Here, also, the majority of findings are grouped about the normal figures for basal metabolism of ±10 per cent and the normal volume per minute of 5.0 to 6.7. The relationship between this and basal metabolism is stricter than that between pulse frequency and basal metabolism but here, too, there occur several sharply variant, disperse values, which indicate that the determination of volume per minute can not be given preference over determination of basal metabolism. We

Table 6. Volume per Minute and Basal Metabolism

	0													
	−	−	−	−	+	+	+	+	+	+	+	+	+	- +
Vol. per min.	30-39	20-29	10-19	0-9	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-x Basal Metabolism %
3.5-3.9		. .	.											
4.0-4.4	.		. . . .	. . .	. . .									
4.5-4.9			. . .	.	. . .									.
5.0-5.4			. . . .	. . . .	. . . .									
5.5-5.9		.	. . .	. . . .	. . . . .	. .	.							
6.0-6.4				. . . . .	. . . .	.	. . . .	.			.			
6.5-6.9				. . .	. . .	. . .	. . . .		.					
7.0-7.4		.		.	. .		.	.	. . . .	.				
7.5-7.9		.			.	.	.	.		.				
8.0-8.4						.		.	.					
8.5-8.9							.							
9.0-9.4	. .					.		.				. .		
9.5-9.9										.				.
10.0-10.4														
10.5-10.9													. .	
	0													

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sought to hold the volume per minute at an approximately constant value by standardization, therefore we commenced with volume per minute per square meter body surface, and thus determined the normal volume per minute per meter for various ages and for both sexes.

$$\text{Meter volume per minute, MMV} = \frac{\text{Volume per minute in liters}}{\text{Body surface in m}^2}$$

We have converted Table 6 in this manner and the volume per minute of each case has been brought into relation with the basal metabolism of the case. This table (Table 7) gives a picture similar to that in Table 6.

This shows also a rather high degree of distribution, so that the meter volume per minute as well as the volume per minute gives an approximate indication of the basal metabolism, but nothing more than this. It is very

Table 7. Meter-Volume per Minute and Basal Metabolism

	0													
M.-Vol. per min.	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-x Basal Metabolism %
2.5-2.9	.	.	. . . .	. . .	. .									
3.0-3.4		.	. . . .	. . . .	. . .		.							
3.5-3.9			. . . .	. . . .	. . . .	. .	. . .							
4.0-4.4		.	.	. . . .	. . . .	. . . .	. . . .	.	.	.	.			
4.5-4.9				. . . .	. .		.	.	. . .					
5.0-5.4		.		. .		.	. .	. .	. .	.				
5.5-5.9					. . .	. .		.		.		. .		
6.0-6.4	.	.												
6.5-6.9							.						.	
7.0-7.4													.	.
	0													

evident that the distribution arises from the varied composition of the expired air.

(*d*) *Relationship between Pulse Frequency and Volume per Minute*

This is in agreement with the general idea that pulse frequency and volume per minute run parallel with one another to a certain extent. This is indicated in the survey table, No. 8. There are some discordant values here also, which originate partly from the inability of certain patients to adjust themselves to unrestrained breathing with the apparatus. Repeated attempts with the same patient brought about a decrease of these extreme values.

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Table 8. Pulse Frequency and Volume per Minute

Pulse	3.5-3.9	4.0-4.4	4.5-4.9	5.0-5.4	5.5-5.9	6.0-6.4	6.5-6.9	7.0-7.4	7.5-7.9	8.0-8.4	8.5-8.9	9.0-9.4	9.5-9.9	10.0-10.4	10.5-10.9 Liter vol. per minute
40-49			•												
50-59	•		•	• •	•	•		•	•						
60-69	•	• •	• •	• • • • • • • • • •	• • •	• • • •	• •								
70-79	•	• • • •	• •	• •	• • • • • • • • • • • •	• • • • • • • • • • • •	• • • •	•				•			
80-89		• •	• •	• • • •	• • • • • • •	• • •	• •	• •	•	•					
90-99		•	•	• •	• •	• •	•			•		•			
100-109				• •	• • •	• •	• • •	• •	• •			•			
110-119						• • •		•		•		•			
120-129					•	•	• •	• • • •			•	•	• •		•
130-139									• •						

Table 9. Respiratory Quotient and Pulse Frequency

R.Q.	40-49	50-59	60-69	70-79	80-89	90-99	100-109	110-119	120-129	130-139 Pulse
To 0.72		•	•	• • • • • •	• •		• • • •	• • • •	• • • •	• •
0.73-0.75		•	• •	• • • • • •	• • • • • •	• • •	• • •	•	• • • • •	
0.76-0.78		•	• • • •	• • • • •	• • • • • • • • • •	• • •	• • • •	•	• •	•
0.79-0.81	•	•	• •	• • • • •	• • •	• • • •	•		• •	
0.82-0.84		• •	• • • • • •	• • • • • • • •	• • •		• •			
0.85-0.87		• •	• • •	• •			•			
0.88-0.90			• • • • •	• • •	•					
0.91-0.93					• •	•				
0.94-0.96			•	•						

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(e) *Relationship between Respiratory Quotient and Pulse Frequency*

What has been said up to the present would imply that, in the matter of thyroid gland pathology, there was a certain association between respiratory quotient and pulse frequency, namely the lowest quotient is to be expected with the highest pulse frequency. The accompanying distribution table, No. 9, brings this out in fact, certainly it has a broad tendency to the lower values. According to the above stated facts, the association would be more disrupted if the majority of diseases of the organs of circulation were investigated.

(f) *Relationship between Respiratory Quotient and Volume per Minute*

In this instance thyroid gland patients possess a certain relationship, in as much as the highest volumes per minute are found with the lowest values for respiratory quotient and *vice versa*. Table 10 demonstrates this, but exhibits a strong tendency to lower values for both factors.

Table 10. Volume per Minute and Respiratory Quotient

R.Q.	3.5-3.9	4.0-4.4	4.5-4.9	5.0-5.4	5.5-5.9	6.0-6.4	6.5-6.9	7.0-7.4	7.5-7.9	8.0-8.4	8.5-8.9	9 0-9.4	9.5-9.9	10.0-10.4	10.5-10.9 Liter vol. per minute
To 0.72		• •	•	• • • • •	•	• • • • • •		• •	•		•	•	•		•
0.73-0.75		• •	•	• • • • • • •	• • • • •	• •	• • • •	• •		•		• •	•		•
0.76-0.78			• •	• • • • • • •	• • • • • •	• • • • • •	• • •	• •	• •	•		• •			
0.79-0.81		•	• • •	•	• • • •	• • • •	• •	• •	•	•					
0.82-0.84	• •	• • •	•	• • •	• • • • •		• •	• • •							
0.85-0.87		•	•	• • •	•		•		•						
0.88-0.90	•	•		• •	•	• • • •	•		•						
0.91-0.93		• •			•										
0.94-0.96							•								

If we ask ourselves now, simply, which of the values derived can be applied for the purpose, at least, of approximate valuation of gas metabolism determination, according to what has been said thus far, pulse frequency, volume per minute and meter-volume per minute are to be taken into account. Pulse frequency exhibits the most accurate parallelism, if we exclude the bulk of thyroid gland material. It ceases to be of value, however, as soon as there arises a question of differential diagnosis between hyperthyroid condition and, for example, a pure cardiac acceleration of pulse. The joint consideration of the volume of breath in thyroid gland cases was determined according to reliable calculation, but it was quite impossible for us to obtain a mathematical formula which, with total constancy of pulse frequency and volume per minute of breath, would give parallelling value for basal

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metabolism. Whether the joint consideration of volume of heart beat (Means, Field and Bock) will yield us any further information, must be obtained by the investigation of a greater number of hyper- and hypothyroid cases. For the present we can say that the determination of basal metabolism can not be obtained by any simple calculation by arithmetical method.

III. Relationship between Basal Metabolism, Body Weight and Body Length

We commenced with the question of whether, in cretins with and without goiter, the body length, namely the degree of dwarf growth, bears any relation to the height of the basal metabolism. The accompanying dis-

Table 11. Body Length and Basal Metabolism (only Cretins)

Body length	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19 Basal Metabolism %
115-119				·		
120-124						
125-129		·	·	· ·		
130-134			·	·	· ·	
135-139		· · ·	·	· · ·	·	
140-144				·	·	
145-149			· ·	·	·	
150-154	·		· · · ·	· ·		
155-159				· · · ·	·	
160-164	·	·	·	·	·	

tribution table, No. 11, shows that such a relation is not evident. Because of the difficulty of performing the gas metabolism experiment on cretins in general, and because of the impracticability of most cretins of Degree III, we do not wish to put much stress on this presentation. At any rate the following fact impressed itself on us:

Cretins with atrophic glands must reckon with a certain lack of gland function in their body. The thyroid gland function which still remains in them is only sufficient for the needs of a dwarf body, rather than for a normal person of their age, for whom the standard tables were constructed. A part of the anticipated deficiency of basal metabolism in a normally constructed adult with acquired myxedema, for example, is here compensated by the arrested dwarf growth. Therefore, the dwarf cretin can possess a "well behaved" basal metabolism if he remains small. Hence arise the compensation processes mentioned elsewhere, which are developed more easily in cretins with thyroid gland insufficiency from youth, than in cases of acute, acquired thyroid insufficiency.

Now we investigated further, whether an association could be demonstrated between basal metabolism, weight and body length, *universally* in thyroid gland material. Indeed the Du Bois formula of body surface is concerned with body weight and body length. This formula, however, refers to *normal* bodies. If we are able to demonstrate a relationship in the distribution table, assuming the correctness of the formula, this must arise from a *pathological* factor. If we consult the body weight from 39 kg. on, which comprises mostly youthful individuals in whom entirely different circumstances are involved, it appears (Table 12) that at the lowest body weights the distribution tends toward the highest basal metabolism and with increasing body weight it is more and more confined to the lower basal metabolic values. The highest basal metabolism and the most intense combustion hence will be found in the thinnest persons. Since this table is concerned only with the thyroid gland, we must recapitulate this evidence and say that a higher basal metabolism with a more rapid combustion of body fat leads to decrease in weight and conversely — a result, then, which was to be expected. In order to

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Table 12. Body Weight and Basal Metabolism

Body Weight	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-x Basal Metabolism %
20-24				·	·									
25-29			·	·	·									
30-34		·	·	·	· ·		·							
35-39		· ·	·	· · ·										
40-44			· ·	· · · ·	· · · · · ·	· ·			· · ·					·
45-49	·	·	· ·	· · · · · · ·	· · ·	·	· ·	·	·	·	·		·	
50-54	·		· · · · · ·	· · · ·	· · · · · · ·	· ·	· · · ·	· ·	·	·			·	
55-59		·	· · · ·	· · · ·	· · · · · ·		·	·		·		·		
60-64			· · · ·	· · ·	· · · · · ·	·	·		·					
65-69			·	· · ·		·	·	·				·		
70-74		·	·	· · · ·	·	·	· ·							
75-79				·										
80-84														
85-89			·	·		·								

estimate the validity of the Du Bois formula, the same kind of calculation must be undertaken for *healthy* thyroid individuals.

Also, the comparison of body length and basal metabolism (Table 13) gives evidence of a certain regularity anticipated from the synthesis of the material. With increasing body length the distribution inclines toward the side of high basal metabolism. For the reliability of the Du Bois formula, the same applies here as above.

IV. Relationship between Basal Metabolism and Rat Test

The rat test according to Asher-Streuli, was undertaken on 40 cases of the material under discussion. Part of these cases are contained in the work of Messrs. Pedotti and Branovacky. The present presentation is an expansion of the latter. The principles on which the comparison is made are analyzed in the above mentioned work, so that we do not need to report them here. We qualify the results as satisfactorily agreeing (even if not always quantitatively parallel), if both the rat test and the gas metabolism are definitely on the plus side, if both hover close to the null line and if, in the case of negative gas metabolism value, the rat injected with arm blood serum reacts with null. (The latter is legitimate since in most cases of minus gas metabolism results, the venous blood from the arm does not influence the rats experimentally.)

We consider the agreement inadequate, for

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Table 13. Body Length and Basal Metabolism (all cases excepting the Group Varia)

Body length	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-x Basal Metabolism %
110-119.9				.										
120-129.9		.	.	. . .	.									
130-139.9		. . .	. . .	. . . .	. . . .									
140-149.9		.	. .	. .	. . .									
150-159.9	.		. . . .	. . . .	. . . .	. . . .	. . . . .	. . .		.	.			.
160-169.9	.	.	. . . .	. . . .	. . . .	. . . .	. . . . .	. .	. . . .	.		. .	. .	
170-179.9			.	. . . .	. . .		.							
180-189.9							.			.				

example, if the rat with a gas metabolism of +20 per cent reacts only weakly positive. We qualify the results as diverging if in the instance of pronounced positive gas metabolism result, the rat does not react positively, or reacts with an abnormally low gas metabolism (under −10 per cent).

Measured according to this criterium, our cases from 40 investigations show

30 times satisfactory agreement = 75 per cent
4 times inadequate agreement = 10 per cent
6 times divergence = 15 per cent

The results agree with those reported by Pedotti and Branovacky and show that the agreement is as broad as may be expected, considering the complex biological methods and the source of error in the nature of the thing itself. An example will serve to illustrate the parallelism of both methods of investigation:

Control No. 106, female patient, 25 years, medium degree of Basedow for 2 years	Basal metabolism	Experiments on rats
9/5/23 (before operation)	+21 %	+++
23/5/23 (12 days after operation, influence of wound resorption)	+14 %	0 to +
13/8/23 (3 mos. after operation)	− 6.5%	0

All three results agree, then, on condition that the one negative result of the rat experiment arose from a profound minus value of basal metabolism.

The relationship between gas metabolism, rat test and tadpole test and the calculation of the rat experiment with arm blood, according to the latest experiments, will be reported by Dr .Branovacky himself in a special article.

(To be concluded)

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Practical Therapeutics

Endocrine Treatment of Retarded or Abnormal Mental Development

DRUG therapy of psychic abnormalities has been notoriously ineffective. The mental diseases are in many instances practically beyond the possibility of any treatment since they arise from a constitutional, hereditary basis. The inherent tendency to react to the environment can not be changed and the evolution of a mature abnormal mind follows a natural course of development, just as certain as the normal type in normal individuals. The course of the classical insanities is therefore marked by an unchangeable progression of well marked, well recognized phases.

The "personality" of the individual is itself a fixed, unchangeable factor so far as the efforts of the physician are concerned. Minor degrees of mental abnormality, erratic behavior not classed as mental disease and border line cases present this constitutional factor as well. Many individuals display peculiar behavior only under stress of adaptation to environment and would otherwise fail to exhibit any abnormality. The physician must always study mental disease from the standpoint of a mental mechanism reacting to the environment.

These constitutional "tendencies" resulting from congenital "psychopathic inferiority" may give diverse symptoms which may make classification of essentially the same types rather difficult. The apparent differences lie either in the different environmental changes to be met or to the different responses to meet them. Underlying is the same abnormal, perverse, instinctive tendency to react to situations in a different manner from "normal" individuals.

Certain types of mental abnormality and conditions of failure of normal development of the mental mechanism have been definitely related to demonstrable defects of endocrine glands. Whether these gland defects are coordinate with other physical retrograde changes or subordinate to more profound changes of constitutional nature can not always be determined. The rather constant association, however, of certain mental defects with specific endocrine dysfunction has been frequently noted.

Moreover, the effect of the internal secretions on tissues and on mind is so great, that even if the ultimate cause lies beyond the endocrine system the actual clinical picture is largely the immediate effect of the abnormal endocrine make-up. No one can doubt the enormous influence on mind and body of the thyroid, pituitary, sex glands or adrenal cortex. Usually more than one gland is involved. The use of such endocrine substances as anterior pituitary, adrenal cortex, thyroid and pineal has a large field of application particularly in those early cases in which deviation from normal is diagnosed and the associated endocrine defect recognized. Delayed mental development with normal characteristics is also a promising field.

Endocrine Dystrophies and Mental Subnormalities. — William G. Downs, Jr. (*Ann. Int. Med.*, **2** : 810, Feb., 1929.)

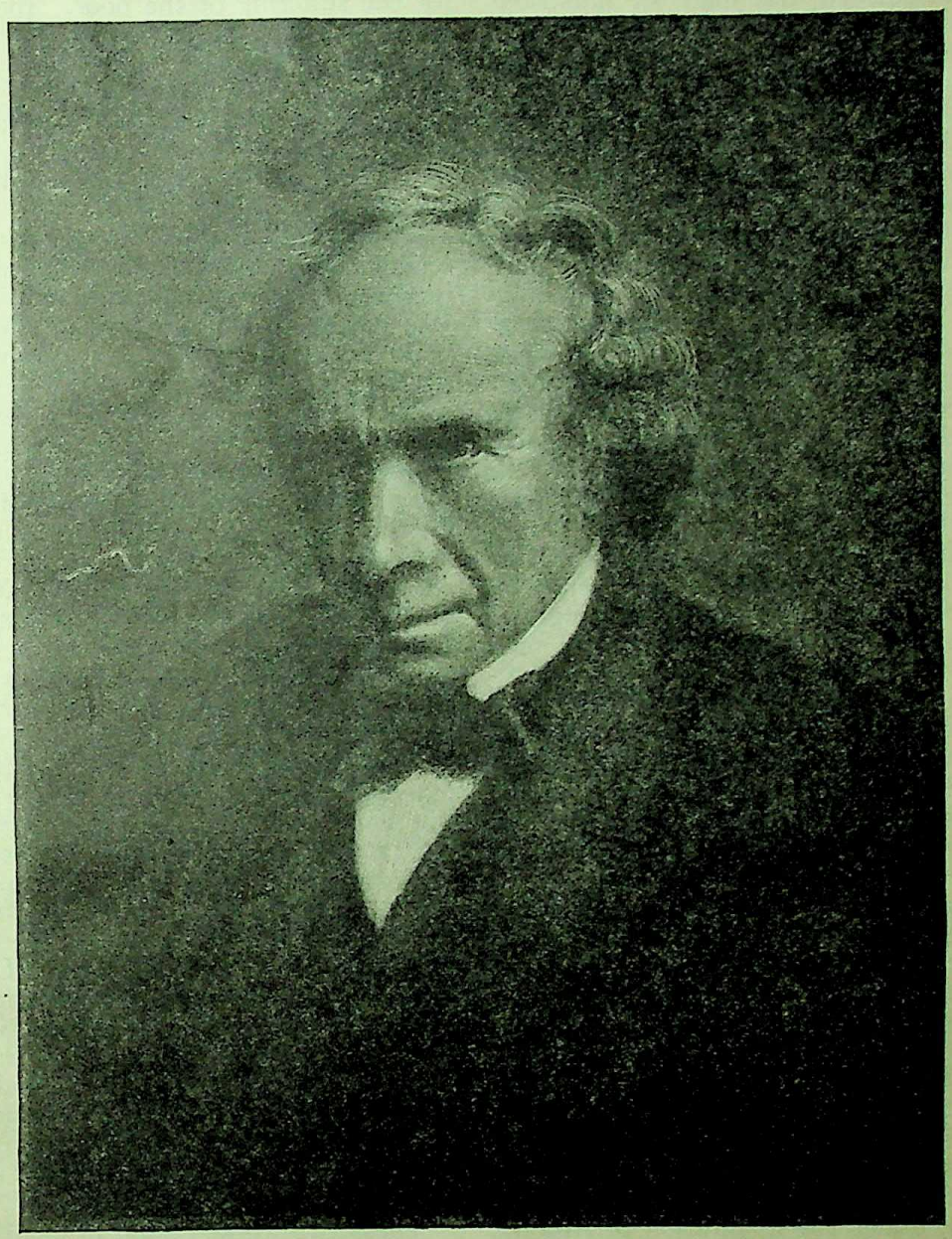
While marked endocrine types are relatively infrequent among the population at large, a very great per cent of the patients in any institution for the care of mental defectives displays unmistakably the symptoms of endocrine defects. As Downs says, it is only to be expected that if the glands of internal secretion have any effect whatever upon the organ-

(*Continued on page 371*)

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The Doctor's Page



WILLIAM STOKES
(1804-1878)

When first meeting William Stokes, Thomas Carlyle described him as a "rather fierce, sinister looking man, . . ." who, as the evening wore on "became more and more gloomy, emphatic, and contradictory." A glance at the accompanying likeness of him, made at about the period when Carlyle met him, seems to confirm such a characterization; but a

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study of the life and work of this great Irish physician discloses a vast difference between his personality and character and his appearance.

William Stokes, son of Whitley Stokes, himself a distinguished Irishman, of illustrious lineage comprising famous engineers, lawyers and public servants since the Norman Conquest, was born in Dublin, July, 1804. His boyhood was spent at his father's country house, Ballinteer, in Dublin hills. William exhibited no special ability as a youth; he was mentally and physically indolent, and the fact that his father was a staunch believer in home instruction encouraged this lackadaisical attitude. He was no athlete: instead of indulging in boy's sports he preferred to hide away in a beech hedge he called his "nest", to while away hour after hour romanticizing over Sir Walter Scott's recently published "Scottish Border Ballads." An incident once occurred, it is reported, which disclosed to him his mother's grief at finding him so disinterested in profound subjects, and virtually overnight he changed into a studious diligent pupil. He admitted later that he had missed much by not receiving systematic college training and he was subsequently a firm advocate of such education. However, there were some benefits to be derived from the education he received at home, for he had the privilege of close association with the reputed scholar and mathematician, John Walker, who was his tutor in Latin, Greek and Mathematics. He also met the distinguished friends of his father's coterie, such as Henry Grattan, Irish lawyer, statesman and orator; James Martineau, English minister and writer; O'Conor, the landscape painter; J. Parsons, eminent lawyer; and Petrie, archeologist, musician and painter, who remained one of his close friends throughout life and whose life he edited and published ("Life and Labours in Art and Archeology of George Petrie").

The first inclination toward a scientific career was evidenced when Stokes made the acquaintance of James Apjohn. From that time forth, under the inspiration of Apjohn, he sought studies in Clinical Medicine at Meath Hospital, in Chemistry in the laboratory at Trinity College and at the Royal Society of Surgeons. For two years he worked in the chemical laboratory of Professor Thompson, and subsequently, on advice from his father, proceeded to Edinburgh for the medical degree. Here he met Professor Alison and chanced to be of some service to him. So great was his admiration for this man that he voluntarily accompanied him night and day as Alison made his rounds. From him Stokes probably derived his sympathy and regard for the suffering of the poor. Eventually in his own practice and clinical work he prolonged the charitable work which Alison had done in the way characteristic of Alison. Nothing was too much for a needy patient who came under his observation, no heart was heavy but that he made an attempt to lighten its burden.

At the period when Stokes was a medical student the French school of auscultation and percussion was in the ascendency. Laennec was having a decided influence on medicine in the United Kingdom. Stokes saw possibilities in the methods and even before he was a fully qualified physician he published (1825) in Edinburgh, a small treatise entitled "Introduction to the Use of the Stethoscope," which netted him £70. This was followed by further contributions on the stethoscope and also to the treatment of diseases of the thorax, which apparently were the foundation for his great treatise on diseases of the chest eleven years later. Several papers on the stethoscope had already been published (especially Laennec's "Mediate Auscultation," 1819), but this work of Stokes was deemed the "first systematic treatise." He was ridiculed by his teacher for devoting himself to the mastery of the instrument, but the success and fame of his later work on the chest attested the sagacity of his study. In the autumn of 1825 Stokes received the degree in medicine at Edinburgh and thereafter was appointed Physician to the Dublin General Dispensary, a post virtually without pecuniary reward, but which he filled to the satisfaction of even the most meticulous. In 1826 an appointment took him to Meath Hospital where he was associated with Robert James Graves, destined to be one of his closest friends and most esteemed companion and associate. Stokes later edited Graves works.

These two worked hand in hand untiringly during the typhus epidemic in Dublin in 1826, as well as in the Asiatic cholera siege which swept Ireland in 1832. Stokes also lectured at Meath Hospital and published many papers in the *London Medical and Surgical Journal*. During 1833 and 1834 the *London Cyclopoedia of Practical Medicine* received from him contributions to Volumes II and III,

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and in 1834 Stokes took up the Editorship of the *Dublin Journal of Medical Science*, to which he brought papers on thoracic pathology in particular. A paper entitled "Peritonitis from Perforation of the Serous Membrane," which introduced the use of opium, and revolutionized the treatment of this disease, appeared between 1833 and 1835. The work on "Diseases of the Chest" actually began in 1835, but on account of ill health, it was intercepted for a trip to the Continent, to Holland, Belgium and up the Rhine. He returned much improved and greatly inspired, with the result that in 1837 this work was offered to an already enthusiastic public and was "hailed with delight" by all classes of scientific workers. Actually in this publication Stokes augmented and corrected the material which Laennec and Corvisart had already presented. The latter two had given, primarily, phenomena of thoracic diseases, so that the minutely descriptive and diagnostic work of Stokes was practically a new and certainly an original treatment of the subject. No one was better qualified than he to systematize the subject matter and to introduce it in excellent language to the English speaking profession. The intelligible graphic terms in which he couched his ideas is still a source of admiration. As a diagnostician he ranks high, for he emphasizes that "physical signs only reveal mechanical conditions which may proceed from the most different causes, and that the latter are to be determined by a process of reasoning on their connection and succession, on their relation to time, *and their association with symptoms*." This book is divided into nine sections; the second, dealing with bronchitis, is reported to be the most exhaustive and voluminous. The detailed descriptions, "a series of living pictures of disease," are invaluable. Englishmen welcomed the work warmly; in Germany it was declared "unequalled since Laennec."

Honorary degrees came in from all sides. He was made Doctor of Medicine in the University of Dublin, Fellow of King and Queen's College of Physicians in Ireland, Honorary member of the Imperial Academy of Medicine in Vienna, of the Royal Medical Societies of Berlin, Leipsic, Edinburgh, Ghent, the Grand Duchy of Baden, of the Medico-Chirurgical Society of Hamburg and of the National Institute of Philadelphia. His works were translated into French and German and revisions were made for American publication. In 1837 the first American edition of "Lectures on the Theory and Practice of Physic" was published in Philadelphia.

To William Stokes credit is due for the founding of a new Society in the United Kingdom: the Pathological Society of Dublin (1838) "not devoted to any school or system, but eclectic, neither regarding morbid anatomy as its first object, but as subsidiary to pathology considered in its widest sense, and embracing the history, symptoms, diagnosis, and treatment of each case of disease submitted to the Society." To the fulfillment of these aims Stokes gave many years of his life and was responsible for unnumbered contributions.

A treatise on "Medical Education," published in Dublin in 1861, is a splendid example of the literary ability with which Stokes pursued each subject he chose. In the same year the honorary degree of LL. D. was conferred upon him by Edinburgh. The University of Oxford in 1865 presented him with the honorary award of D. C. L. and in 1874 the Royal Irish Academy inaugurated a new institution by electing Stokes, a physician and the first to be chosen for this post, president. Ill health, however, permitted him to serve for two years only, after which he resigned. One other rank of distinction must be mentioned, namely that of Regius Professor of Medicine at the University of Dublin, which came to Stokes after the death of his father (1845).

Besides a successful teacher and writer Stokes was a matchless story-teller, a born conversationalist. His writings, whether scientific or literary, were expressed in excellent English; his letters to his family and friends, while he travelled over the Continent, are virtually literary gems in their beautiful descriptions of the things he saw and the people he met. His Celtic wit is refreshing and characteristic. Shakespeare and Scott were his chosen writers. He was well versed, not only in the works of these men but also in the poetry and folklore of his own and other countries.

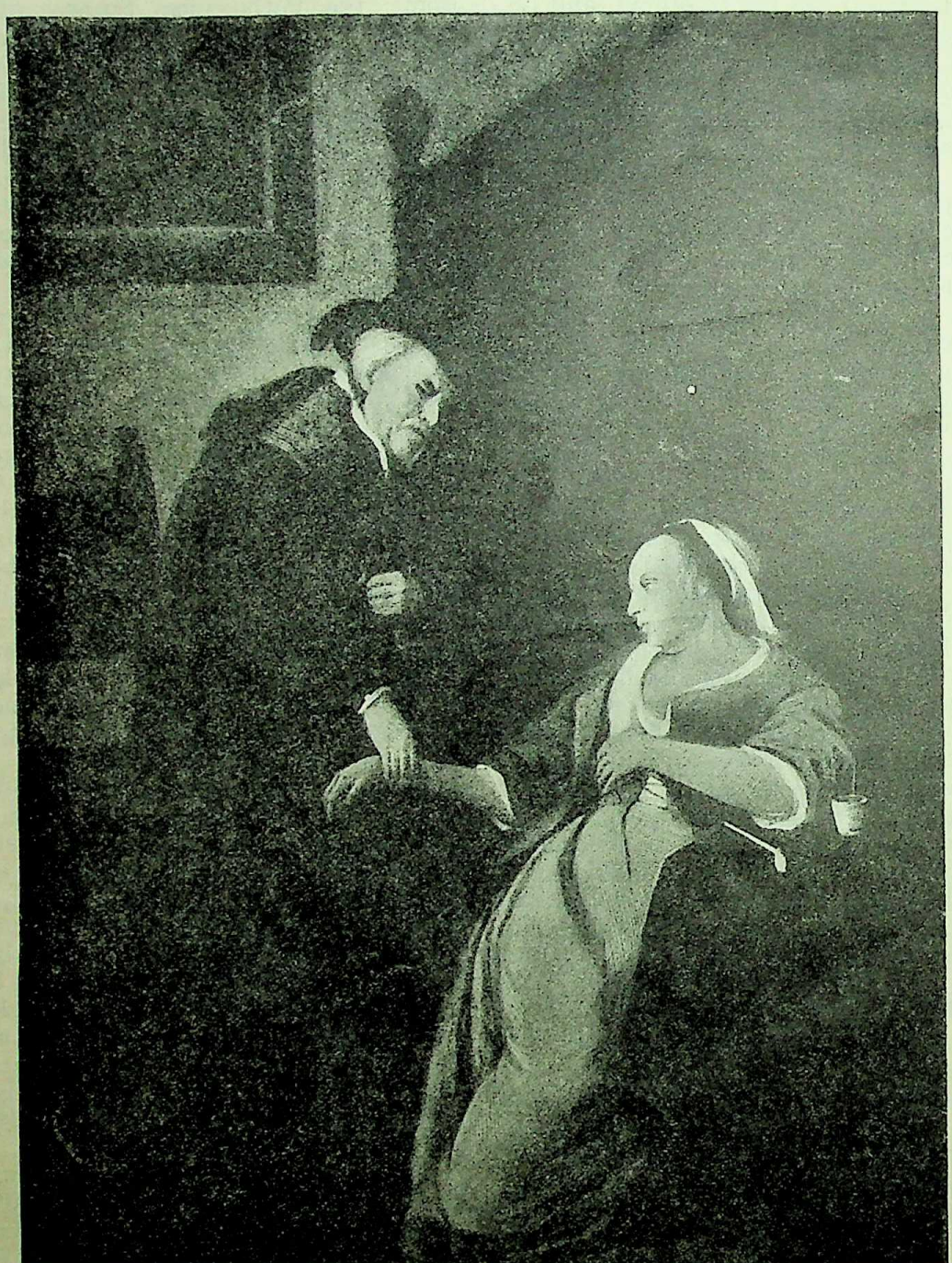
The home life of the Stokes household must have been ideal, with such a fascinating host to preside. The family circle was very close, for Stokes was exceptionally fond and thoughtful of his wife and children; he gave them unusual opportunities to meet and enjoy illustrious and interesting persons who visited the house for evenings of diversion. There

(*Concluded on page 374*)

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Medical Subjects by Famous Masters



"A DOCTOR FEELING A PATIENT'S PULSE," by Jan Havicksz. Steen (1626-1679)

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Editorial Comment

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Suprarenal Cortex and the Secondary Sex Characteristics

SOME relationship of the suprarenal cortex to the secondary sex characteristics, both to their development and to their subsequent maintenance has long been recognized. Deficient sex development is found to be frequently associated with small cortex; sexual precocity with cortical hypertrophy; changes in the cortex occur during estrus; feeding the gland increases the rate of growth of the testes; and most spectacular of all, the curious change from the secondary sex characteristics of the female to those of the male (virilism) are constantly found to be associated with neoplastic growths of the cortex. Riddle found the weight of the cortex constantly increased at each ovulation cycle, an increase averaging 40 per cent. L. C. Wyman found that suprarenal insufficiency in rats results in partial or complete inhibition of estrus, the extent of the insufficiency being directly related to the degree of disturbance of the ovarian function. R. C. Moehlig gave experimental evidence to show that the cortex is fundamentally related to the development of all mesothelial tissue and that both development and subsequent normal function of the sexual glands are dependent upon the normal functioning of the suprarenal cortex. Hartmann and his associates have demonstrated that these effects are due to a hormone by extracting a potent substance which they call "cortin." With this substance animals in which the cortex has been removed may be kept alive and by the use of subminimal amounts the symptoms of suprarenal insufficiency may be maintained.

Abstracts of articles by F. Ricci and by L. Langeron, E. Decherf and Danes appear below. They are typical of many which have been previously reported and are rather striking cases of this curious influence of the adrenal cortex on sex.

Suprarenal Virilism. — F. Ricci. (*Il Policlinico*, Oct. 1, 1928.)

After a review of the cases of this affection already reported, F. Ricci reports the case of a woman of 34 years who presented simultaneous crises of pain in the right hypochondrium with lumbar irradiations, a disappearance of menstruation and appearance of abundant hair on the chin and upper lip, then on the abdomen and legs; at the same time the voice became heavier. There was noted edema of the lower members, a collateral lumbar circulation and of the subumbilical, and palpation revealed the presence in the right hypochondrium of an elastic tumor, of unequal consistency, distinct from the liver, and heavy. The spleen was hypertrophied and hard. The liver slightly enlarged; the urine slightly albuminous; examination of the blood showed nothing abnormal outside of the presence of some myelocytes and neutrophil metamyelocytes. Catheterism of the right ureter was possible only to a length of 20 cm. and pyeloureterography showed a sudden elbow in the region of the third lumbar. Operation disclosed a tumor as large as the head of a fetus,

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enclosing the kidney, which was, however, distinct from it. Upon section it presented degenerated zones and zones having the appearance of fish meat. The patient died the evening after the operation.

Histological examination showed that this tumor had all the characteristics of a suprarenal tumor; it presented polymorphous elements, with large elements in the midst of ordinary cells, with hyperchromatic nucleus and with protoplasm of cylindrical form. There were also giant multinucleated cells and necrotic cells interposed between the well preserved cells; the stroma was represented exclusively by blood capillaries as is the rule in suprarenal tumors. Finally the cells with nuclear fragmentation and karyokinesis confirmed the malignant character of the tumor.

The author shows the interest of this case which confirms the existence of relations between the suprarenal and the development of secondary sexual characteristics.

Suprarenal Cortex Epithelioma with Virilism and Hirsutism. Localization by Pneumoperitoneum. Surgical Extirpation. — L. Langeron, E. Decherf and Danes. (*Bull. et mém. Soc. méd. hôp. Paris*, **45** : 436, Apr. 1, 1929.)

The rarity of suprarenal tumors induced the authors to report the following case: virilism, amenorrhea, hirsutism, hypertension, glycosuria, and emaciation in a young girl of 20 years; localization by pneumoperitoneum of a tumor in the left suprarenal region; surgical extirpation, sudden death 36 hours after the intervention; histologically: suprarenal cortex epithelioma.

Abstracts

Contributions to Ovarian Transplantation after Loss of Both Sex Glands. — Siegert. (*Med. Klin.*, **25** : 1808, 1929.)

For the most part autoplastic ovarian transplantation has not brought about the expected result. Symptoms of insufficiency of various sorts could not be ameliorated, nor could menstruation be induced. The test with injections of substance from the anterior lobe of the pituitary to stimulate the function of the sex glands was unsuccessful. According to clinical experience with the cases observed it must be assumed that the implanted tissue is more or less decomposed and that it is hence impossible to substitute for the loss of the ovaries in sexually mature women.

The Influence of the Female Sex Glands on Obesity. — Wagner. (*Zeitschr. ärztl. Fortb.*, **26** : 781, 1929.)

The sex glands predestine certain skin reactions in obesity. Hence a constitution factor is concerned in the existence of obesity. Of 500 women castrated by the roentgen ray method 300 took on weight and of these 200 gained 5 kg. Investigations by Kaufmann have shown that after injection of highly potent sex gland hormone the fat content of the blood is definitely increased, and thus the fatty acid phosphatides are increased; on the other hand, the cholesterin ester is not.

Organotherapy in Neurology. II. Special Report. — Josef Wilder. (*Der Nervenarzt*, **2** : 656, 1929.)

The advantage of synthetic preparations is their totally constant capacity and the entire certainty of dosage; the disadvantage is that they contain not the active, but rather the most active principle for the gland concerned. In substitution therapy the synthetic preparation is often surpassed by the natural gland product (Addison's disease, myxedema).

Adrenalin: There is a widespread opinion that adrenalin is unimportant; this is not true. The author observed very definite effects with doses of 20 drops of a 1:1000 solution or after a tablet, even though they were much weaker than after the same dosage was administered parenterally. Natural products seem to contain hypotensive substances (Roger) particularly the watery extracts. With regard to individual sensitivity it must not be forgotten that the body weight of the patient must be taken into account.

In amyotrophic lateral sclerosis Schacherl emphasizes testis. In arthropathia deformans

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an endocrine subgroup which reacts to ovarian preparations, is certainly present.

In cardiac asthma pituitrin is allowed by many authors.

Angina pectoris should react favorably to administration of parathyroid (Peritz).

Many ovarian preparations were tested in chlorosis. Appert found these ineffective and recommends, on the other hand, the administration of testis to women. Blondel, Marcolango and others reported upon thymus as an effective medium.

Pal recommends and administers very small adrenalin doses, orally, in cardiospasms, especially after mealtimes.

Brünn observed success with posterior lobe of the pituitary in dyspnea and also in cases of cardiac and emphysematous dyspnea. In hypertonia thyroid is recommended by Jagic, Januschke and Molnar. In essential hypertonia Kylin recommends sex gland and the author, too, experienced success with sex gland medication in such cases.

In cephalea of nasal origin adrenalin often gives brilliant results. In myalgic form (Peritz) sex gland therapy and eventually thyroid is suggested.

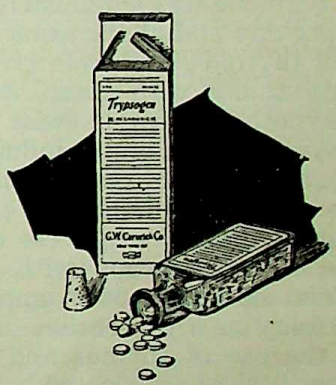
Reports on Post-Operative Treatment. I. Post-Operative Gastrointestinal Paresis and Atony. — Ed. Melchior. (*Der Chirurg*, **1** : 1198, 1929.)

One of the oldest peristalsis-inducing mediums is the hormone derived from the spleen by Zuelzer and Dohrn, which is actually able to exercise a very considerable stimulation on the intestinal tract. Nevertheless, the preparation does not meet with favor because of the occurrence of the usual unpleasant secondary symptoms as evidenced by cold chills and imminent conditions of collapse. The extracts of the posterior lobe of the pituitary form the most active and most applicable substances for the institution of a regular post-operative peristalsis. Their effect extends into the large intestine as well as into the small one. One disadvantage of this preparation lies in the large dosage, wherewith conditions of collapse are likewise imminent. However, the administration of pituitary preparations can not be recommended warmly enough. One important fact is that the action is not restricted to intestinal factors, but also they possess a tonicizing effect on the general circulatory apparatus, one which closely resembles a prolonged adrenalin effect.

The Idea Behind the Product

UNDERLYING the treatment of diabetes today is the conception of a deficient secretion of the pancreas. Experiment and clinical experience have shown that diabetes is a complex disease and not simply due to lack of a single internal secretion. Several internal secretions elaborated by the pancreas as well as the enzyme have been clearly shown to be lacking.

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New Views on Liver Diseases from the Internal and Surgical Standpoint. — P. F. Richter. (*Zeitschr. ärztl. Fortb.*, **26** : 782, 1929.)

The therapy of disturbances of liver function has the task of supplementing the function by means of glycogen administration, in parenchymatous injury the simultaneous construction and fixation of glycogen in the liver must be derived by means of insulin. The chief realm for insulin-sugar therapy is subacute and chronic cases of icterus. Richter recommends relatively small doses of insulin (10 to 20 units twice per day) with the richest possible carbohydrate diet.

Recent Advances in the Therapy of Nervous and Mental Diseases (Exclusive of Fever Therapy). — Alexander Pilcz. (*Wien. med. Wochenschr.*, **79** : 1507, 1929.)

In the treatment of various myopathies investigations with consequently conducted organotherapy, especially in dystrophia muscul. progress. were promising. In males the sex gland hormone was administered three to six times per day and at the same time small amounts of thyroid gland were given. Cases of pituitary tumor with conspicuous symptoms of hypothyroidism likewise had their pituitary symptoms favorably influenced with thyroid medication (for example, disturbances of sight) which is very important practically. In Raynaud's disease a process of thyroid medication in combination with sex gland hormone and pituitary, often appears especially necessary as a preventive. In morbus basedowi the use of thymus and sex gland preparations besides arsenic and bromide may be recommended. In tetany the expectations have not been entirely fulfilled with regard to preparations of epithelial substance. In many tick-forms of adolescent individuals a combined thyroid-sex gland medication brought about very good results. Dosage with other sex gland preparations, however, gives slight success.

In mental diseases with sitophobia insulin injections have proved very effective because the patient is again brought to spontaneous ingestion of food on account of a strong feeling of hunger aroused.

In psychoses of the group schizophrenia organotherapy is capable of accomplishing something in new cases (catatonics and hebephrenous forms) (Kauders). In female individuals with deferred or faulty development of puberty organotherapy causes not only initiation of sex maturity but also cure of the psychosis.

Discussion on the Subject of Alkali Therapy of Acidosis. — Meyer-Bisch. (*Zeitschr. ärztl. Fortb.*, **26** : 778, 1929.)

Acid secretion of the stomach and pancreas secretion run parallel. In each case of achlorhydria the pancreas secretion must be treated simultaneously. If the acid secretion must be decreased the ensuing pancreas defect must be simultaneously paralyzed.

Investigations on the Threshold for the Medium Influencing Diuresis with the Help of Intrarenal Injection and Reduction of Kidney. — Hans Molitor and P. Nikoloff. (*Arch. exp. Path. u. Pharmakol.*, **145** : 331, 1929.)

The inhibition of diuresis occurs neither more abruptly nor more strongly with intrarenal injection of pituitary extract than with subcutaneous injection.

After subcutaneous injection of pituitary extract the inhibition of diuresis occurs at once, but lasts only for a short time.

Following intracisternal injection of pituitary extract an inhibition of diuresis occurs which is similar to the effect with intravenous application in abruptness and with the subcutaneous effect in duration. For the diuresis-inhibiting effect of pituitary extract in intact and unnarcotized animals there is no evident genuine renal threshold.

On the Effects of Pituitrin and Insulin on the Secretion and Blood Vessels of the Isolated Adrenals. — M. P. Nikolaeff. (*Naunyn-Schmiedebergs Arch. exp. Path. u. Pharmakol.*, **140** : 225, 1929.)

The limits of concentration of pituitrin which no longer effects secretion of the medulla substance of the isolated organ are about 1:1,000,000,000. Insulin acts analogously to pituitary substances, only with insulin the secretion is longer taking effect and hence lasts longer. With continuous transfusion the effect ceases. The effect on the vessels consists of a vasodilatation and an additional constriction with pituitrin solutions from 1:1000 to 1:10,000. The insulin-blood vessel effect pursues a slightly regular course.

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Concerning the Blood Sugar-Active Substances in Secretin Extracts. — H. Heller. (*Arch. exp. Path. u. Pharmakol.*, **145** : 343, 1929.)

There are contributions which state that the stimulation of the internal secretion of the pancreas may result from one of the hormones sent into the blood from the intestinal wall.

Oehme and Wimmers, Takaye, Zunz and others state that the intestinal secretin has a blood sugar-decreasing effect.

The author made common salt extracts from the intestinal cortex of rabbits and tested their effect on normal and heightened degrees of blood sugar. These extracts lower the hyperglycemia after peroral and intravenous glucose administration and permit the succession of hypoglycemia. Fasting blood sugar was slightly decreased by the extracts. The adrenalin hyperglycemia was influenced in the same way as the alimentary. The active principle of the extract is identical neither with histamin nor cholin. The active extract may be obtained only from the mucous membrane of the duodenum or the upper jejunum. The extract when administered gives a negative biuret and xanthoprotein reaction, Millon weakly positive, Pettenkofer test for bile acids and Gmelin test for bile color negative, Pauly test intensely positive. The substance is stable against cooking, the question of identity with secretin could not be set aside without objection. It was shown that insulin was not contained in the mucous membrane of the upper intestinal tract.

Report on Liver Therapy Particularly in Combined Treatment with Arsenic. — Hans Hollmann. (*Deut. med. Wochenschr.*, **55** : 1834, 1929.)

On the basis of his experiments the author was able to offer a combination of arsenic with liver extract for the treatment of anemia. While arsenic, through stimulating the blood-forming centers increases the production of red blood corpuscles, the liver extract, on account of its detoxicating effect, inhibits the premature disintegration of the formed red blood corpuscles. The indication for introduction of arsenic-liver therapy is not confined to pernicious anemia alone, but may be widely applied; for instance, chronic streptococcus infections, associated with secondary anemia, seem to be favorably affected with arsenic-liver treatment.

Studies on the Mechanism of Adrenalin Glycosuria. — J. E. Holst. (*Zeitschr. klin. Med.*, **111** : 761, 1929.)

Since earlier investigations on the mechanism of adrenalin glycosuria did not give any definite conclusions, the author conducted other experiments on this subject. In 8 test persons (1 normal, 1 case of ulcus ventriculi, 1 case of renal glycosuria, 1 case of morbus basedowi and 4 diabetics) calculations of values were plotted on curves, partly after subcutaneous adrenalin injection and partly after glucose administration. The tests justify the assumption that the mechanism of adrenalin glycosuria is of the same sort as that of alimentary glycosuria.

Inverse Hormone Effects. — G. Katsch. (*Med. Klin.*, **25** : 1723, 1929.)

In repeated intravenous administration of small doses of hormone in short intervals of time, effects may occur which can be deemed the opposite of the recognized proper effect of the hormone concerned. By means of very small doses of insulin the author was able to effect a long continued increase of blood sugar in an animal experiment. The amounts of hormone administered would have induced intense drop in blood sugar if given at one time in one dose. These observations are important but they do not influence the practical therapy of diabetes.

Skeletal Muscle Extract As a Tonicizing Medium. — J. S. Schwarzmann. (*Wien. klin. Wochenschr.*, **4** : 1513, 1929.)

As a result of favorable effects with skeletal muscle extract of the calf in angina pectoris the author tested the influence of this on various other disease conditions such as hypodynamia, in nervous exhaustion, in conditions of fatigue, in reconvalescents after acute infectious diseases, in diseases associated with psychic depression, in impotentia sexualis, in individuals with restricted capacity of the heart muscle and in dyspnea after slight movements, as well as insufficiency of the myocardium with disturbances of compensation.

In all these disturbances the muscle extract exercised a general tonicizing effect in that it greatly increased the capacity of the patients and brought about a state of euphoria.

That the author has met the necessary requirements for the exclusion of the possibil-

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ity of a suggestive effect, need not be especially emphasized.

The effect of the extract was shown in a very pregnant manner in neurotics who complained of a feeling of oppression in the breast and need of air. In cases in which, owing to sluggish heart activity, movements brought about slight dyspnea these conditions were greatly ameliorated with the extract.

However, in patients with very pronounced insufficiency of heart muscle and disturbances of compensation, the general conditions as well as the dyspnea symptoms were greatly improved under the exclusive influence of the extract, without any further therapy.

The objective findings show that heart tonus, particularly weak previous to injection, is often strengthened in a manner not to be undervalued.

In a single case in which the patient received digitalis, there were indications to support the idea that muscle extract administered simultaneously strengthened the effect of digitalis. This, however, is a problem which must have further study.

Calf Thymus and the Maintenance of Carcinolysis and of Blood Formation in Inoperable Carcinoma. — Alois Kittinger. (*Wien. klin. Wochenschr.*, **42** : 1434, 1929.)

From exhaustive investigations the author draws the following conclusions:

1. The capacity of blood serum for the release of isolated carcinoma cells may be increased by means of transplantation of the thymus of the calf or thymus injections, if it has totally disappeared. Yet a lasting condition was never obtained.
2. The thymus substance given is effective when transplanted, or given by injection or by enema.
3. Disturbance of health can thus proceed from or depend upon the decomposition of the albumin molecule.
4. The formation of blood could not be influenced continuously. An eosinophilia was never obtained.

Concerning the Failures of Liver Therapy in Funicular Diseases of Pernicious Anemia. — F. Krause. (*Klin. Wochenschr.*, **8** : 2177, 1929.)

From the four case histories presented it was shown that the number of red blood corpuscles promptly rose to over 3 millions with liver therapy, and in Cases 2 and 4, even over 4 millions. Nevertheless, the nervous symptoms grew worse, particularly in the first and fourth cases the spinal symptoms were so severe that the disease process in the bone marrow looked as though it would be fatal. At the same time, it must be brought out that the general condition of the patients was definitely improved in all cases, with liver therapy, so that there was no question of a severely cachectic, bed-ridden individual.

The Relation between Parathyroid and Thyroid Glands and Skeletal Growth. — V. Lasas and Z. Mozkus. (*Anat. Anzeig.*, **68** : 113, 1929.)

The growth of the skeleton in dogs (in the first month of life) was inhibited by means of total extirpation of the thyroid gland. In instances of coincident removal of the parathyroid the inhibiting effect on the skeletal system was more plastic. The growth in length was particularly intercepted.

Concerning the Administration of Pituitary Preparations in Kidney Diagnosis. — Ferdinand Liebermann. (*Deut. med. Wochenschr.*, **55** : 1879, 1929.)

As has long been known, in water tests on healthy individuals pituitary preparations inhibit diuresis during the first hour with notable rise in concentration. This obstruction to diuresis is to be observed in slight degree of injury to the kidneys, in kidney diseases without kidney insufficiency. The concentration capacity is not so great, however, that the hypophysin test can take the place of the thirst experiment entirely. In cases of kidney insufficiency with hyposthenuria the inhibition of diuresis is often lacking, and particularly in associated increase of concentration. The evidence of Kerppolas that there are cases of pronounced kidney insufficiency in which the tolerance for hypophysin was to be considered as evidence of the concentration capacity of the kidney requires further proof.

Organotherapy with Spleen in Tuberculosis of the Lungs. — (*Monde méd.*, **38** : 966, 1929.)

In the Hérold Hospital from the year 1926 to the end of March, 1928, twenty-six children underwent spleen therapy. The following results were thus obtained. With regard to weight, in a single case there was a drop. In 3 cases the increase in weight amounted to

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more than 10 kg., in 3 cases to more than 8 kg., in 5 cases more than 4 kg., in 3 cases more than 6 kg., in 2 cases more than 4 kg., and in 1 case more than 1 kg. The bacilli disappeared in 10 cases; they remained in 12 cases, of which one, however, showed an unheard of decrease in number. The roentgen picture exhibited a clearing up in 12 cases, no clearing in 11 others. In all cases in which a blood corpuscle count was made, there was evident a remarkable and permanent improvement in red blood corpuscles. In all cases in which the calculation was made a significant increase in proportion of hemoglobin occurred. Of the children observed there were 12 with evening temperature between 38.6° and 40°, 8 of these were fever-free, 4 exhibited a fall to 38°. As the end-result of 26 cases 4 instances of death were reported, 1 case of exacerbation, 4 improvements, 7 striking improvements and 10 cures, or such an improvement that the patient is considered to be on the road to recovery.

The Feeding of Spleen in Suppurating Diseases of Bone and Joint. — F. Löffler. (*Zentr. Chir.*, **56** : 2946, 1929.)

The author administered a mixture which was given in soup in amounts of about 3 tablespoons per day. Children with very severe tuberculosis were treated, intensely fistulizing bone and joint diseases which had been treated for months previously with other methods.

Locally, cessation of the fistulization occurred. Diminution and reddening of the granulation, cessation of edematous swellings and pressure pains were obtained. The general condition was strikingly improved. Also, children with severe chronic osteomyelitis, in whom well defined sequestration of the bone had not yet occurred, were treated successfully with spleen preparation.

On the Action of a Hormone of the Anterior Lobe of the Pituitary on the Release of Milk Secretion. — F. Grüter and P. Stricker. (*Klin. Wochenschr.*, **8** : 2322, 1929.)

The investigations of the authors on the influence of a hormone of the anterior lobe of the pituitary on the secretion of milk gave the following results. A hormonal substance is contained in the anterior lobe of the pituitary which can exercise a particularly stimulating effect on the mammary glands and which most certainly causes the release of the secretion of milk at the moment of birth. Other organ extracts such as those from liver, lung, posterior lobe of the pituitary and even the placenta have exhibited negative results in this respect, even though they have been given in doses much higher than in the experiment cited. The milk-increasing effect of placenta extracts is often quoted. One of the authors studied this problem in 1920. In cows which were experiencing lactation, whether after bearing or several days after ovariectomy, it was possible to obtain a degree of improvement in milk supply with ingestion or subcutaneous incorporation. However, it seems that the influence of the anterior lobe of the pituitary is more effective. Besides it was never possible to initiate lactation with placenta extracts, and indeed the authors who were able to provoke milk secretion could only do so after many weeks of repeated injections.

Metabolism Experiments in Pernicious Anemia. I. Contribution. Basal Metabolism and Liver Diet. — K. Grassheim. (*Zeitschr. klin. Med.*, **111** : 601, 1929.)

From observations and clinical experiments in thirty cases of Morbus Biermer it follows that very severe disorders of metabolism may be present when an obvious total remission is effected by means of liver diet. Hence one can not speak of an absolute cure with liver diet.

Oral Spleen Therapy in Polycythemia. — U. Friedemann and H. Deicher. (*Klin. Wochenschr.*, **8** : 404, 1929.)

As an outcome of the work of Lichtwitz and Francke the authors report on procedures with a spleen preparation in a case of polycythemia. From their tables it is evident that after administration of spleen tablets the hemoglobin values fell from 95 to 85 and the erythrocyte counts from 6,200,000 to 4,150,000. On the day following the introduction of spleen tablets (29/IX) the hemoglobin values rose again to 97, the erythrocyte count to 5,470,000. In the following table the values also remained high, on the average, and finally reach the initial values observed, again. Unfortunately the authors were unable to make more recent tests of the results of spleen therapy, for the patient left the hospital. In the authors' experiments a definite influence on erythrocyte count and on hemo-

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globin values in polycythemics seems to be presented through spleen therapy.

Date	Hemoglobin (Sahli)	Erythrocyte Count
20/XI/1927	100	5,900,000
21/XI/1927	95	5,600,000
22/XI/1927	110	4,900,000
23/XI/1927	104	5,100,000
24/XI/1927	..	.....
25/XI/1927	..	.....
26/XI/1927	98	4,690,000
27/XI/1927	..	.....
28/XI/1927	95	4,440,000
Spleen tablet medication commenced		
29/XI/1927	85	4,150,000
30/XI/1927	97	5,470,000
1/XII/1927	108	5,600,000
2/XII/1927	97	6,160,000
3/XII/1927	103	5,820,000
4/XII/1927	96	6,250,000

The Diuresis-Promoting Effect of Liver Extract in Dogs with Insufficient Kidney. — Susi Glaubach and Hans Molitor. (*Wien. klin. Wochenschr.*, **42** : 1438, 1929.)

The diuresis-promoting fraction of liver extract is present in a powder which is easily soluble, in cold, in physiological salt solution and has a diuretic effect on dogs in amounts of 1 to 2 mg. per kg. The subcutaneous injection of it is rather ineffective. Secondary symptoms were never observed either locally or generally. Intravenous injection, which was incidentally tested, acted no better than the subcutaneous, and was quite free from secondary symptoms. The blood pressure of decerebrate cats was only slightly depressed with the preparation so that the histamin content of the substance is negligible. The substance is free from bile acids and lipoids and very poor in albumin. Its salt content can not be the cause of the diuresis-promoting effect, for the control tests with the incinerated product were without effect on water metabolism. Only so much of an increase in urine will be derived as there is substance in the liver which could be transferred into the extract. Tests with such a strong purin derivative as theophyllin have often shown that the subcutaneous injection of 0.01 to 0.02 gm., hence an amount 10 to 20 times greater than administered liver extract, remained entirely without effect on the urine.

What the nature, chemically, of the diuresis-promoting substance is, is not yet known. Just as little can be predicted as to why a substance derived from the liver is so effective in an oliguria with genuine renal dependence. It must be remembered, however, that there are a number of older experiments according to which an incretion of the kidneys, Nephrotoxin, formed particularly in atrophying kidney tissue, is capable of injuring the liver, specifically, and also the kidney itself.

Whether the diuresis-promoting principle will also be demonstrated in human beings as a useful therapeutic medium in renal and other disturbances of water economy, experiments first must instruct us.

The Influence of the Thymus on Growth under Normal and Abnormal Conditions. — Leon Asher and Pierin Ratti. (*Klin. Wochenschr.*, 8 : 2051, 1929.)

There exists a series of viewpoints on the fact that the thymus has an influence on growth. For the recent investigation of this function, always more and more restricted, growth experiments were conducted on very young rats. In the first series animals were fed under optimal conditions. The one series of very young rats received a diet consisting of milk and bread, the other series received the same diet, and simultaneously, at definite intervals, intramuscular injections of thymus extract, and also, thymus was ingested. The growth in the latter series was very abrupt and intense. Hence it was concluded that in very young animals the addition of thymus to the diet, and particularly the parenteral injection furthers the growth process. More significant for the effect on growth, however, are such tests as experiments conducted under unfavorable conditions. For such condition the rickets diet of McCollum was chosen and the animals were kept in the dark. Two series were arranged. The one, of young rats, was placed in a glass chamber (Bern metabolism cage) and received the diet inducing rickets exclusively. The other series received the same diet, but to every three animals, collectively, 30 gm. of fresh thymus was also given. Both series were kept away from light. The control series developed a typical severe rickets. The other animals receiving thymus, however, developed in a normal manner. The microscopic investigation which Professor Wegelin was kind enough to do in the thymus animals, presented evidences of normal rib

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and femur epiphyses besides rib fractures. From these experiments it is shown that the addition of thymus can totally offset the effect of a rickets-promoting diet. Whether the thymus gland acts as a substance to improve nourishment or hormonally, further experiments must determine.

Concerning Blood Pressure Disturbances in Morbus Basedowi. I. Blood Pressure Increase and Instability of Height of Blood Pressure. — E. Barath. (*Zeitschr. klin. Med.*, **111** : 718, 1929.)

It is not yet decided what importance is to be ascribed to an increased thyroid gland activity and the change of blood pressure niveau. The expressed juice of the thyroid gland appears to exercise a depressive effect on the blood pressure.

v. Fürth and Oswald have shown that the intravenous incorporation of thyroid gland preparations increases the effect of adrenalin injections. On the other hand Falta and Newburgh, and Nobel and Pilz found a decrease in blood pressure if large amounts of thyroid substances were ingested. The author investigated the changes in the blood pressure curve induced by thyroxin in therapeutic doses, in healthy persons, but could not determine any definite effect of the medium on the blood pressure values. Thyroid ingestion offers no uniform explanation of the conditions of disturbances of equilibrium in the blood pressure system.

Concerning Blood Pressure Increase and Certain So-Called Hypoglycemic Conditions following Insulin Injections. — A. Brems and Cai Holten. (*Bibliothek f. Laeger*, **121** : 463, 1929.)

The authors present experiments for the determination of an alteration in secretion of adrenalin following insulin injections, in normal and diabetic persons.

Rise in systolic blood pressure was observed in normal as well as in diabetic individuals. The increases seemed to occur only in those cases in which "hypoglycemic" symptoms, in the form of vasomotor symptoms, were observed, while in all other cases the blood pressure remained uninfluenced, even though the blood sugar exhibited a very intensive drop.

The rise in blood pressure and the "insulin condition" were in direct parallel. The rise in blood pressure, apparently, is dependent upon adrenalin activity brought about by insulin through the splanchnici with central irritation.

This central irritation is to be traced partly to drop in blood sugar. The hyperadrenalinemia incurred after insulin injection must be influenced by the glycogen-mobilizing effect modifying the insulin-blood sugar effect.

Circulation Hormone and Internal Secretion. — E. K. Frey. (*Münch. med. Wochenschr.*, **76** : 1951, 1929.)

The blood contains large amounts of hormone. On the basis of a clinical finding (operative) the author determined the interrelationship between the internal secretion of the pancreas and the substance found in the urine. After total extirpation of the pancreas the hormone content of the urine is decreased about 80 per cent in a short time. During a 2 hour clamping off of the pancreas blood vessel, the amount of circulation hormone in the urine is significantly decreased, after release of the flow through the organ again it increases. The circulation hormone may be derived from the pancreas tissue in large amounts. From 1 gm. of pancreas substance the author derived 50 units of active substance. Doubtless the hormone is the basis of many other effects, which appear to proceed particularly from the spleen. With removal of the spleen the hormone content of the urine drops off rapidly and intensely. The author assumes that the hormone-activating substance is formed from the lymph glands; by means of 1 gm. of lymph gland 500 units of the circulation hormone can be rendered inactive.

The Nerve Disturbances of Biermer's Anemia and Liver Therapy. — H. Curschmann. (*Med. Klin.*, **25** : 1689, 1929.)

The impression gained from statistics of an obvious accumulation of spinal complications in pernicious anemia following institution of liver therapy is to be directly explained (in part) through success of liver therapy. Previously, the presence and progression of the spinal symptoms were overshadowed by the disease picture of the general state of cachexia. Now, following liver therapy, with a blood finding at least representing a picture of temporary cure, the patient presents an opportunity for the special consideration of the symptoms which can not be influenced with liver therapy. In the failure of liver treat-

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ment in the spinal syndrome of pernicious anemia it would be premature to draw any theoretical conclusions, on the one hand, concerning the premise that liver action is not a vitamin effect, as Stepp has propounded, that on the other hand, liver therapy is only a symptomatic treatment of the blood injury, but not an etiotropic combatant of the cause of the entire disease condition. However, the experiments give evidence of the fact that the funicular myelitis of the Biermer patient requires a particular treatment; if the fever cure treatment is applied here it must be remembered that this therapy, of course, must be instituted only after total compensation of the blood injury is effected with liver preparations.

On the Question of the Pathological Changes in the Internal Organs of the Dog after Introduction of a Spleen Pulp Emulsion into the Blood (Experimental Investigations). — T. Chorunschenko. (*Zeitschr. ges. exp. Med.*, **64** : 185, 1929.)

On the basis of his animal experiments the author comes to the following conclusions.

1. Disintegrating spleen tissue possesses toxic properties.
2. If spleen emulsion be introduced into the blood, a general effect is produced in the organism in the form of a degeneration in all parenchymatous organs.
3. The toxic effect after introduction of an emulsion of spleen tissue is evident equally as much whether the spleen originates from the same or another animal.
4. If the spleen is present in the animal organism, the emulsion introduced has a less harmful influence than after splenectomy. It is possible that the spleen existing in the organism produces substances by means of which the disintegration products of spleen tissue may be neutralized.

Osseous Lesions in a Myxedematous Cretin Dwarf. — Berard. (*Presse méd.*, **37** : 39, Jan. 9, 1929.)

The author reports a case of a man of 39 years, measuring 1.10 meters, with the usual history. The interesting part of the observation is a series of radiographs which show articular lesions and a persistence at certain points of the connecting cartilages. In addition there exist osseous dystrophic lesions which resemble those of fibrous osteitis.

DYSMENORRHEA

The demonstration of the influence of the several hormones of the ovary on menstruation is one of the brilliant achievements of endocrinology. The estrus-stimulating follicular hormone and the inhibiting hormone of the corpus luteum in conjunction with the hormone of the anterior pituitary and of the adrenal cortex form a delicately balanced mechanism controlling menstrual flow, changes in vaginal and uterine mucosa and general metabolism. Slight defects in this mechanism as a whole or of its individual endocrine gland components give rise to irregularities of menstrual process of which pain at the menstrual period is a conspicuous symptom.

In treatment this endocrine mechanism may be stabilized with

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On the Pathology of the Endocrine System. — G. Döderlein. (*Beitr. path. Anat. u. allg. Physiol.*, **83** : 92, 1929.)

Disturbances of the internal secretions, especially functional disturbances of the thyroid gland not only diminish the total value of the sperm cells of an adult individual to total sterility, but they also injure the fetus in the pregnant mother (animal experiments) during the particularly sensitive epoch of embryonal development. This sort of sperm injury in the fetus, however, in the absence of definite morphological evidence of the impregnation capacity or incapacity of the sex germs, first comes to light in the age of sex maturity, as a lack of function. Hence precaution can not be advised too much in the administration of endocrine gland products in pregnancy. Every endocrine therapy which does not serve exclusively to remedy the existing insufficiency of internal secretion causes a disturbance of the equilibrium. Mother and child are a biological unit. Growth regulating hormones, to which the thyroid gland hormone also belongs, act on the fetal organism in its initial development much more intensively than on the adult body of the mother. Whether harm ensues, or whether the endocrine disturbance can be smoothed out without trace is merely a question of degree of disturbance in the experiment, and with therapeutic administration, a question of dosage. For the assay of natal endocrine disturbance, however, the phenotypic appearance alone is not sufficient. The endocrine system only assumes its full function after puberty, when the sex glands are incorporated. With regard to the full value of these, however, only the genotype evident from the generations decides the probability above all of a latent injury.

On the Treatment of Diabetes Insipidus with Pituitrin and Vasopressin in Endonasal and Subcutaneous Administration. — A. W. Elmer and M. Scheps. (*Münch. med. Wochenschr.*, **76** : 1917, 1929.)

Pituitrin as a snuff powder has a favorable effect on diabetes insipidus and should be considered the method of choice.

The endonasal administration of pituitrin as snuff powder requires larger dosage than the subcutaneous application. The endonasal treatment is to be preferred over the injection method, not alone because of agreeableness, but also because of the long lasting pituitrin resorption and the avoidance of unsatisfactory secondary symptoms resulting therefrom (increased blood pressure and anuria).

The endonasal administration of pituitrin snuff powder is to be preferred to pituitrin tamponade treatment, since the latter requires more technique, the tamponades must be changed every six hours in order to avoid irritation of the mucous membrane, and pituitrin in tamponades is more difficultly resorbable and requires greater dosage. Vasopressin injected subcutaneously acts more strongly than pituitrin, but causes unsatisfactory accessory symptoms: body weakness, headache and stomach ache, nausea and diarrhea. Vasopressin treatment by means of tamponades is not suitable for long treatment.

In endonasal treatment with vasopressin no secondary symptoms appear.

Blood Sugar-Decreasing Extracts from Human Organs. — H. Brugsch. (*Zeitschr. ges. exp. Med.*, **65** : 574, 1929.)

The investigations in dead organs for their insulin content must be performed with the consideration that these can quickly deteriorate after death, and particularly the pancreas. The values found decrease greatly and appear to be especially dependent upon the state of nutrition. Thus, the pancreas of an individual dead from starvation contains no insulin, while the musculature and heart are still rich in content. In the main, the collective musculature contains much more insulin than the pancreas, whereas the liver, spleen and kidneys contain as much or less.

Comparative Experiments on the Activity of Synthetic Thyroid Gland Preparations. — Lisbeth Auerbach and Béla Klein. (*Klin. Wochenschr.*, **8** : 2332, 1929.)

Much has been done on the subject of the effect of thyroid gland preparations in healthy persons. Unity of opinion on the question has not been reached as yet. While the opinions regarding native preparations are in accord, for, one can, even if not in all cases, at least with a normal amount of surety, call forth hyperthyroid symptoms until thyrotoxicosis is attained, the reports concerning pure thyroxin and on its effect on the organism read very variously. Experiments were made with preparations from different manufacturers and the activity was tested with regard to weight tables, diuresis curves, metabolism and basal metabolism. In gen-

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eral, then, a result was noted with subcutaneous and intravenous application methods which was quite variable only quantitatively. But with peroral dosage there were extensive divergences, in that one series of investigations gives contradictory results concerning their activities, or gives evidence of a minimal effect; another, however, affirms them and partly coincides with the above mentioned processes.

For the first test series which was assayed with preparations from other concerns the authors investigated thyroxin in the form of ampoules and drops, and were able to confirm a definite thyroid gland effect in the organism. A parenterally administered dose of 3 times 2 mg. approximately agrees with double the amount of ingested thyroxin. The authors will report further, in another place, concerning the other test series, and on the literature up to the present time.

Insulin, Synthalin and Glukhorment. A Comparative Investigation concerning Their Effect on Glucose Fixation through Cells. — E. Salén and T. Nyrén. (*Acta med. scand.*, **69** : 69, 1928.)

An investigation was made to determine whether the action of insulin in increasing glucose fixation, noted by the Graz School, in the blood cell experiment, is a specific effect for insulin. The experiments carried on by the authors with synthalin and glukhorment under similar experimental conditions show a qualitatively identical effect in increasing glucose fixation for these two substances as for insulin.

It is to be assumed that this effect is entirely conditioned by the synthalin-like substance present in glukhorment. This effect in increasing glucose fixation belongs also to the chemically pure substance, synthalin.

The proof that synthalin *in vitro*, even in a completely insulin-free medium, exerts an action in increasing glucose fixation which harmonizes with that of insulin seems to suggest that synthalin has a direct and primary effect on sugar regulation.

The Action of Insulin on Regeneration. The Biological Rôle of Potassium and Calcium Ions in This Process. — B. A. Schazillo and M. Ksendowsky. (*Pflügers Arch. ges. Physiol.*, **220** : 774, 1928.)

The experimental results of the authors support the favorable action of insulin and calcium ions on the formation of callus. From Repinous and Leberts' investigation it may be seen that insulin introduced into the body effects a shifting of the acid and base equilibrium towards the side of the acids. Through this shifting callus regeneration is promoted (according to Abderhalden). On the other hand, introduction of calcium incites the central stimulation of the vagus nerves, which increases insulin production in the pancreas. From this it may be concluded that insulin (as pancreas internal secretion and insulin-like substances present in the body fluids) combined with potassium and calcium ions, not only plays an important biological rôle in the transformation of substances, but also in the formation of structure elements. At any rate it may be gathered from the results of the authors' experiments that insulin when it is introduced into the body, increases bone regeneration.

Concerning the Action of Hormones, in Particular of Pituitrin on the Vasomotor Centers. — Ch. Inalea. (*Zeitschr. ges. exp. Med.*, **63** : 523, 1928.)

The author was able to corroborate the finding of Spiegel and Saito, that the injection of doses (0.1 to 0.2 cc.) of pituitary extract, inactive intravenously, into the lateral ventricle in rabbits, may cause a slight fall of blood pressure, concerning which, however, it must be emphasized that the action of pituitary preparations is exceedingly inconstant. The author's experiment speaks in favor of the idea that the pituitary product on its way through the ventricle in the subarachnoid space rather exerts a slight action on the diencephalon center in the sense of the incitement of a vasodilation, whereas it scarcely seems to influence the rhombencephalon centers.

Hemorrhage following Delivery: Medical Treatment. — Varon and Chavent. (*Bull. obstét. et gynécol.*, No. 9 : 869, 1928.)

In a patient with spontaneous delivery which was terminated within 40 minutes and with apparently, absolutely complete placenta, an abundant hemorrhage suddenly appeared on the fifth day following delivery. In addition to hot vaginal irrigations, subcutaneous injection of post-pituitary extract was made and calcium chloride was administered internally. On the following day another hemorrhage. No more hemorrhage followed; the patient was discharged cured after 12 days.

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Hemorrhages in the Menarche. — F. Kermauner. (*Wien. med. Wochenschr.*, **78** : 1511, 1928.)

Hormone treatment strives for a causal attack with the ultimate end of a cycle regulation. The author tested a great number of the procedures proposed with patience and perseverance. He tried treatment in the form of oral administration and of injection intravenously and intramuscularly. The author was unable to determine any great differences in the manner of action of the various ovarian preparations on the market. They were all useful in certain cases and all failed in more severe cases. In milder cases a trial of one of these remedies is indicated. In the future the author will use only a treatment with ovarian preparations by mouth, in the form of suppositories or at any rate through administration of intramuscular and subcutaneous injections; in no case, however, will he choose the intravenous route. The author also hopes to obtain better results when more active preparations are at his disposal than at the present time. On the other hand, in cases of hyperthyroidism, a truly causal administration of thyroid tablets or thyroxin or small doses of iodin is instituted. Among the remedies for symptomatic therapy the author counts blood transfusion, calcium and pituitary preparations in treatment of these hemorrhages.

A Case of Pituitary Infantilism. — G. Roussy, J. Bollack and Kyriaco. (*Presse méd.*, **37** : 21, Jan. 5, 1929.)

The authors present a case of pituitary infantilism where the early visual symptoms drew attention to the disorders of development. The patient was a child of 12 years, of very well developed intellect, presenting height, weight and dentition of a child of 7 years, despite the existence of normal points of ossification for his age. The sella turcica is very much enlarged but the clinoid apophyses were respected. Vision of the right eye, which had been failing for the past 2 years, had become almost negative and the papilla was atrophied. Vision of the left eye was normal despite very definite temporal narrowing of the visual field. There were no signs of intracranial hypertension nor of diabetes insipidus nor of adiposogenital syndrome. The authors come to the conclusion that it is a case of pure infantilism of pituitary origin, of Souques and Chauvet's type, due probably to an intracranial tumor.

Endocrine Preparations. — Schemensky. (*Münch. med. Wochenschr.*, **75** : 1783, 1928.)

In various endocrine disturbances (at the climacteric, in pluriglandular infantilism, in endogenous obesity and male castration) the author was able to obtain favorable clinical results with fresh substances of the glands in question (testis - ovary) as well as with the corresponding endocrine preparations.

The Search for Adrenalin in the Suprarenal Capsules, post Mortem. — L. Langeron and P. Lohéac. (*Rev. franç. endocrinol.*, **6** : 347, Oct., 1928.)

The search for adrenalin in the suprarenal capsules has but a speculative interest. Physiology teaches us that suprarenal extracts are hypertensive and the recent works of Tournade and Chabrol have shown the rôle of the suprarenal secretion of adrenalin in the maintenance of arterial tension.

The authors have undertaken their investigations in order to determine what contribution the search for adrenalin can bring to this theory: Whether there is a relation between the tension observed during life and the rate of adrenalin in the suprarenals after death; under what conditions and by what technique should this research be practised in order that the results be as certain as possible.

The authors conclude that in order to ascertain exactly the amount of adrenalin in human suprarenals these organs must be removed as rapidly as possible after death, 2 to 3 hours at the most and they must be placed in the sulphuric vacuum as soon as possible. The dosage should take place after 24 hours in the vacuum. Dosages which are not made under these conditions have no great value, for the absence of adrenalin in the suprarenals at autopsy may be due to the influence of cadaverization. Moreover, an examination of the suprarenals removed very soon after death would give only the amount of free adrenalin and not the amount of total adrenalin.

The results of authors, who have practised these dosages under defective conditions can not be retained. Of course, the rapidity of death certainly influences the amount of adrenalin in the suprarenals. The results are, however, at least comparable among themselves. At the present time, in the absence of a great number of dosages effected under these conditions, it is impossible to know whether there is a constant relation between

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the amount of adrenalin of the suprarenals and the tension observed during life.

The precise conditions under which such researches should be instituted are not such as to render them very frequent or very easy. One does not often have occasion to make autopsy on patients with hypertension. Thus, in two patients with hypertension, whose vasculorenal apparatus was sufficiently healthy for the hypertension to be considered solitary or essential, and who died rapidly of cerebromeningeal hemorrhage, the authors found the amount of adrenalin to be 0.39 gm. and 0.06 gm. per 1000 gm. of gland, and this same amount (0.39 gm.) was also found in a cachectic tuberculous patient with hypotension. It would, therefore, be premature to draw conclusions. However, the authors found an interesting indication which again brought up the question of the relations between arterial tension and suprarenal adrenalin, in the following fact: Of two suprarenal tumors, one hypertensive and the other with normal tension, the first was found to be especially rich in adrenalin, while the second was entirely deprived of it. The observation is not unique and more precise indications on the subject may be found in Lohéac's thesis, etc. If, therefore, in a general way it is admitted that neoplastic tissues possess to an exaggerated degree the properties of the elements from which they have issued, the condition favorable to the study of these phenomena may be found in this exaggeration itself.

However it may be, the search for adrenalin in the suprarenal capsules, *post mortem*, is capable of giving results which appear to be interesting, but only under the technical conditions enumerated in this article.

Regarding Edema of the Face at Menstruation Time, of Endocrine Origin, in a Heredosyphilitic. — J. Gaté and J. Rousset. (*Presse méd.*, **36** : 1481, Nov. 21, 1928.)

The patient, an Algerian, aged 27 years, menstruated normally at 11 years and became amenorrheic at 18 years. Her menstrual periods are characterized by discomfort and very marked facial edema, accompanied by sensations of burning, and lasting 5 to 6 days. Her urine was normal. The various functional tests of the endocrine glands revealed a definite hypothyroidism with dysthyroidism and sympathicotonia which become exaggerated at the time of menstruation. This patient is an hereditary syphilitic. Thyro-ovarian treatment associated with arsenobenzol caused the discomfort to disappear, in particular the menstrual edema.

Pituitary Dwarfism. — Lucke. (*Münch. med. Wochenschr.*, **75** : 1783, 1928.)

In a 6 year old child with pituitary dwarfism the author was able to obtain a very good growth-furthering effect by anterior pituitary therapy continued for a long period of time.

The Hormone of the Female Sex Glands. — F. Siegert. (*Med. Klin.*, **24** : 1479, 1928.)

The hormone production in the ovary is at its height immediately before and during menstruation. The production sites are not only the maturing follicle and the corpus luteum but also the cells of the theca interna. In pregnancy, the hormone formation is still essentially raised but is, however, managed only in small part by the ovary and in large part by the placenta. The action of the sex gland hormone is not species specific but sex specific, that is, it extends only to the genital zone. Although the hormone certainly effects the setting in action of the growth effect, this growth stimulation does not extend to the sex glands. It is neither possible to bring about an enlargement of the ovary nor the maturation of a follicle through the estrous hormone. On the contrary, the maturation of the follicle is inhibited by the hormone. The very noteworthy property of the hormone is its ability to restrain the male sex function. In this case it is not merely a temporary cessation of spermatogenesis, but also a retrogression of the testis, penis, prostate and seminal vesicles.

Portion of the Pituitary and of the Hypothalamus in Experimental Diabetes Insipidus. — P. Trendelenburg. (*Klin. Wochenschr.*, **7** : 1679, 1928.)

Following removal of the pituitary a not inconsiderable amount of a substance appeared in the tuber cinereum, which acts on the excretion of urine in a similar manner to that of the posterior lobe of the pituitary, and which is present in the tuber cinereum of normal animals in but slight amounts. (It is likewise the same with a uterus-stimulating substance.) Diabetes insipidus is possibly of pure hormonal nature: when the delivery of the urine-inhibiting substance in the posterior pituitary lobe is lacking, the tuber cinereum enters vicariously, and only after its destruction does

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the maximal, no longer reparable diabetes insipidus develop. This theory explains in entirely satisfactory manner all hitherto irreconcilable results of experimental diabetes insipidus in animals.

Influence of the Glands with Internal Secretion on Bone Metabolism. — Stracker. (*Med. Welt*, **2** : 1544, 1928.)

The author used the Abderhalden reaction in diseases which are associated with atrophy, and in arthritis he observed increased decomposition of thymus, parathyroid and ovary. These are, for this reason, therapeutic organ preparations.

Rosacea and Its Treatment. — O. R. Stein. (*Wien. klin. Wochenschr.*, **41** : 1382, 1928.)

The rosacea zone of the face in the female sex is under the influence of the genital sphere. During menstruation the sexually mature woman inclines to outbursts of rosacea, which may become stabilized with the appearance of the menopause. It is, therefore, logical to treat post climacteric rosacea (whose genesis is certainly to be attributed to the disturbed ovarian function) by administration of ovarian preparations and to control the active hyperemia of the climacteric as well.

The Function of the Spleen in Healthy and Diseased Organisms. — R. Siebeck. (*Zentr. Chir.*, **55** : 2324, 1928.)

It has been observed at various times that the resistance of the red blood cells increases following extirpation of the spleen. In any case it may not be mistaken that loss of the spleen signifies a marked stimulation for the bone marrow. It has been assumed that the abolition of some hormone inhibiting the bone marrow, perhaps of the sinus endothelia, asserts itself here. Otherwise also, observations have been undertaken in support of the assumption of special spleen hormones. That the spleen cooperates in digestion is admitted; Schiff has conjectured that the spleen is involved in the formation of trypsin. A pepsinogenous function of the spleen was especially maintained by Tarulli and Pascucci. Other authors refer to a peristalsis-furthering hormone in the spleen. Perhaps these effects are to be explained (Bayer and F. Schulze) by a hormone of the spleen affecting the autonomic nervous system, the vagus. A report is also made concerning the relations of the spleen to other hormonal organs, to the thyroid, thymus, sex glands, etc.

The Influence of the Chronic Administration of Insulin on the Suprarenals in the Rabbit. — H. Langecker. (*Nauryn-Schmiedebergs Arch. exp. Path. u. Pharmakol.*, **134** : 154, 1928.)

The suprarenals of rabbits chronically treated with insulin are on the average heavier than in the normal animal. This applies as well to the absolute value as to the living weight per kilogram. The differences are great enough for the assumption of the origin of a chronic suprarenal hypertrophy through chronic administration of insulin, with due regard for the standard deviation. The adrenalin content which is to be determined colorimetrically is unchanged, so that it may be assumed that the reducing elements of the suprarenals, which are genetically related to adrenalin, may in no way be influenced. The hypertrophy of the suprarenals which arises in the course of chronic insulin treatment in rabbits is largely to be attributed to the cortex.

Treatment by Ovarian Hormone of a Case of Scleroderma. — P. Harvier and A. Lichtnitz. (*Paris méd.*, **18** : 483, Dec. 1, 1928.)

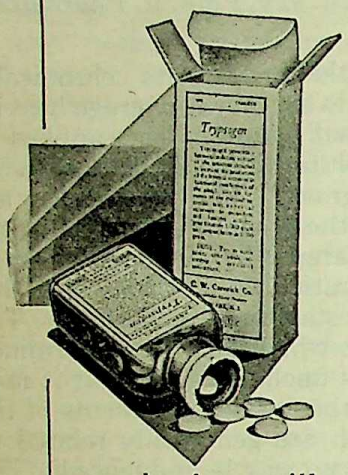
Among the numerous theories seeking to explain the pathogenesis of scleroderma, the endocrine-sympathetic theory is the most frequent. The thyroid, suprarenals and pituitary have successively been held responsible according to whether the scleroderma was associated with or followed goiter, myxedema, exophthalmic goiter, various pituitary syndromes, or coincided with cutaneous pigmentations attributed to a disturbance of the suprarenal functions. A number of authors have observed improvement in their patients following thyroid, pituitary or combined organotherapy. The possible rôle of ovarian insufficiency in the genesis of scleroderma has almost always been relegated to the background.

However, the observation which the authors report is that of a young girl affected with scleroderma of progressive evolution, associated with menstrual disorders and which though not influenced by thyroid and pituitary therapy, was rapidly ameliorated, if not cured, by ovarian organotherapy. The scleroderma had not passed the sclero-edematous

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stage, and was limited to the cheeks, neck, arms, thorax and upper part of the abdomen. Occurring in a girl of 23 years, coinciding with signs of ovarian insufficiency, an evident amelioration followed injections of ovarian hormone.

Although various authors mention ovarian insufficiency in the course of scleroderma, the majority of authors seem to deny it the primary rôle and consider it as a consequence of other endocrine lesions, in particular thyroid lesions. In the authors' patient, there was no sign of hyper- or dysthyroidism. On the contrary, the menstrual disorder appeared from the installation of the scleroderma and has persisted after it. After successively trying without result acetylcholine, pituitary and thyroid organotherapy without observing the slightest local change, the authors had recourse to ovarian organotherapy because of the retardation of menstruation which appeared in the first month following the onset of the scleroderma. It must, accordingly, be recognized that ovarian organotherapy employed alone caused a rapid regression of the cutaneous affection.

The Therapy of Acne Vulgaris. — G. Stümpke. (*Zeitschr. ärztl. Fortb.*, **25** : 692, 1928.)

In cases of acne vulgaris which are related to a dysfunction of the thyroid, the application of ovarian preparations is recommended by Dóczy. In this respect favorable and unfavorable reports appear in the literature. The author himself observed a brilliant result in a 16 year old girl with unusually obstinate acne of the face, following 7 weeks of treatment with one ovarian tablet three times daily and later 4 tablets three times daily, finally with injections of ovarian hormone, which, however, was later weakened by a relapse. In a second case, the complete retrogression of a severe, disfiguring, infiltrating acne of the face was obtained in a 17 year old patient following 15 injections of pituitary extract, and no relapse occurred during further observation for several years. In a 25 year old patient with disfiguring affection of the face and raised metabolism, treatment with Antithyroidin Moebius effected a cure. The author has had little experience with combined preparations and considers the administration of single endocrine substances — when an indication to combined therapy is present — more to the purpose.

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The fact of the appearance of acne vulgaris during the period of development, its coincidence with irregularities of the internal genital organs, the observation of slight sexual needs in these patients, simultaneous change of other endocrine organs (thyroid, suprarenals), observations concerning the calcium content of the blood and anomalies of the hair, point to changes in the whole organism and for this reason require a corresponding therapy.

Investigations concerning the Action of Alkaloids Similar to Adrenalin: Ephedrin and Synthetic Ephedrin.—L. Takács. (*Wien. klin. Wochenschr.*, **41** : 1375, 1928.)

The alkaloids, ephedrin and synthetic ephedrin (whose activity is not lessened by oral administration) raise the blood pressure similar to adrenalin. The rise in blood pressure lasts much longer than that induced by adrenalin and is a result of contraction of the vessels, which is conditioned by the stimulation of the peripheral sympathetic nerve endings. The evacuation of the stomach is delayed by ephedrin and synthetic ephedrin. The influence on the gastric secretion is dependent upon the state of equilibrium of the vegetative nervous system and renders possible the ascertainment of a rise in tonus of the parasympathetic system. Therapeutically, ephedrin has been used successfully in the abortion of and prevention or alleviation of asthma attacks and for the relief of bronchial dyspnea.

Joint Disease and Sex Glands. — J. Wiesel. (*Wien. klin. Wochenschr.*, **41** : 1425, 1928.)

Genital disturbances have been described by various authors in acute joint rheumatism, such as cessation of menstruation, exacerbation during menstruation, etc. In girls whose puberty shows rather a hypothyroid course, a pubertal arthropathy is found. These girls also exhibit disturbances of the equilibrium of the endocrine glands, such as severe accumulations of fat through ovarian hypofunction, acroparesthesias, etc. Pains in the joints are also to be observed during puberty in the forms which can be designated as hyperthyroid. Clinically, the course here is somewhat similar to that in the climacteric. A considerable number of authors have described the exceedingly frequent occurrence of chronic deforming arthritis in the climacterium. Roentgen findings, which are in some degree characteristic, are found in particular in the second form of the climacteric, chronic, deforming joint diseases, Heberden's nodules, concerning whose endocrine cause scarcely a doubt any longer exists. Similar pictures can be experimentally produced following removal of the sex glands.

Treatment of Pernicious Anemia with Liver Substance. — C. S. Engel. (*Med. Welt*, **2** : 1644, 1928.)

The property of the liver as exclusive blood forming organ for the red blood cells in the embryonal period induced the author to recommend and use already 3 decades ago embryonal and fetal livers of mammals as remedy in severe anemias.

Such a preparation must contain the nuclein organically combined in the nucleus and phosphorus in similar organic combination, since the bone marrow always produces only erythrocytes with nuclei. It is important that the liver with a lecithin content of 2.1 per cent is a substance richest in lecithin in the body next to egg yolk. Liver appears, accordingly, especially suitable to rebuild the stroma, that is, the supporting substance of the erythrocytes. The statement that the extract of liver substance, furthering the building up of red blood cells, is free from lecithin and lipoids, does not seem suitable to the author. Engel considers it as necessary in the first place to introduce substances of various types into the organism, if the bone marrow is to be stimulated to blood formation in increased degree.

Experiments with Antithyroidin Moebius in Post-Operative Tetany. — A. Zaloscer. (*Med. Klin.*, **24** : 1344, 1928.)

The existence of a functional relation between thyroid and parathyroids can be designated as proved; also from positive observations the conclusion is justified that the hormones produced by both glands are antagonistic to each other. Walbaum and Rudinger assume that the favorable action of Antithyroidin in exophthalmic goiter is to be attributed to a large content in parathyroid hormone, which opposes the pathological increase of thyroid function. If this theory is correct, a direct substitution therapy must be possible with Antithyroidin, that is, this must also prove to be effective in post-operative tetany following strumectomy. Pro-

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ceeding from this consideration, the author gave Antithyroidin in two cases in which pronounced tetanic manifestations appeared following struma operations. In both cases a positive objective result was effected through treatment with Antithyroidin Moebius.

General Viewpoints in the Treatment of Diabetes Mellitus. — T. Weihs. (*Münch. med. Wochenschr.*, **75** : 1764, 1928.)

The author recently had a patient under treatment who showed such a marked cutaneous reaction to insulin that the further treatment with insulin became impossible. Change of the preparation and intramuscular injection did not alter it in the least. Nevertheless, untoward effects of insulin seldom appear and insulin represents a valuable enrichment of diabetes therapy. Of course, there are a series of preparations which are said to influence diabetes favorably, all of which however, can not replace insulin. Synthalin is to be mentioned as being undoubtedly active. It lessens polyuria, lowers blood sugar and in the easy dosage of 20 to 40 mg. causes the disappearance of 20 to 40 gm. of sugar from the urine. The secondary effects are, however, underestimated. It is obviously not a question of dyspepsias but of pronounced toxic manifestations. The longest period of toleration for synthalin which the author has observed amounted to 4 months. Staub also gave a very unfavorable judgment concerning synthalin at the last congress on metabolism. The new remedy, Glukhorment, is only an imitation of synthalin. Fornet's insulin pills to be taken orally are, in the opinion of competent authors and in the author's personal opinion, inactive. The substances present in several plants (garlic) which lower blood sugar, have so slight an effect that too large amounts of the substance concerned would be necessary.

Concerning Regulatory Processes in Experimental Hyperthyrosis. — J. Abelin and R. Vuille. (*Endokrinologie*, **2** : 248, 1928.)

In experimental hyperthyrosis in animals, prophylactic measures of the organism assert themselves at the same time with the metabolic lesions. These measures are aimed at directing the abnormal course of the metabolic process again into physiological paths and to counteract the rise of the resting metabolism, the excretion of nitrogen and the specific dynamic action. This becomes especially distinct in sugar metabolism. The latter suffers great changes under the influence of the first feeding of thyroid substance, in that the glycogen-forming ability of the liver is completely lost while that of the muscles is lost to a certain degree. This severe attack on the carbohydrate metabolism leaves, however, a considerable protection against a repeated similar injury. With later repetition of the administration of thyroid substance, the liver no longer loses its ability for glycogen synthesis and the glycogen formation in the musculature remains normal.

Pituitary Posterior Lobe Extract Action on Fat Metabolism and the Vegetative Nervous System. — W. Raab. (*Zeitschr. ges. exp. Med.*, **62** : 366, 1928.)

The fall of the value for the petroleum fraction in the blood regularly caused by pituitrin is dependent upon a lowering of the neutral fat content in it. This pituitrin effect is weakened by ergotamin or removed by atropin; on the contrary, not essentially harmed. Ergotamin and atropin in themselves show no characteristic influence on the blood fat content. The influence of pituitrin on fat metabolism proceeds by way of the tuber cinereum — cervical spinal cord — sympathetic — liver.

Contribution to the Study of the Resuscitation of the Heart and Respiration in Severe Narcosis Incidents. — B. Ronzini. (*Policlinico, Sez. Chir.*, **2** : 90, 1928.)

The favorable adrenalin effect in such cases can be supplemented with success by the vagotropic atropin action, since atropin makes it possible for the amphotropic adrenalin to produce an exceedingly energetic and purely sympathetic action through suppression of the vagus function. Through addition of pituitrin the elective stimulating effect is exerted on the cardiac muscle fiber and in order to induce respiration, lobulin can be added with advantage.

Calcium Investigations in Skeletal Diseases. — Barrenschien and Gold. (*Wien. med. Wochenschr.*, **78** : 1340, 1928.)

The parathyroid hormone prepared by Collip effects an essential rise in blood calcium and an increase in calcium excretion through the urine. Large doses of parathormone lead

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to the typical disease picture of hypercalcemia, in which the experimental animals die in a comatose condition with abnormally high blood calcium values. The action of the parathormone must thus be conceived as a mobilization of the calcium deposits from the tissues. The picture of osteitis fibrosa generalisata of Recklinghausen shows an extensive agreement with the experimentally established inundation of the organism with the hormone of the parathyroids.

Concerning Recent Researches on the Action of Post-Pituitary Preparations and Their Significance in Practice. — A. Leimdörfer. (*Wien. med. Wochenschr.*, 78 : 1197, 1928.)

Following an intravenous injection of pituitrin a rise in blood pressure occurs. Following injection of pituitrin there results a retention of water, an increased condition of swelling of the tissues and thereby a diuresis inhibition, a decrease of water excretion through the kidneys. Pituitrin administered intravenously is often accompanied by good results in post-operative or peritonitic intestinal paralysis. Through its diuresis-inhibiting element, pituitrin renders valuable services in certain disturbances of circulation, namely in attacks of cardiac asthma or pulmonary edema. Injected subcutaneously or intravenously, (1 cc.) pituitrin can frequently be of great service, improve severe attacks, remove danger to life for the moment. Since, moreover, pituitrin is a highly active agent by intralumbar use to influence the blood pressure center directly and so induce a rise in blood pressure from the center, one will endeavor to raise this central fall in blood pressure through intralumbar injection of a good pituitrin preparation in certain disease conditions in which a central fall of blood pressure occurs. In this respect, acute infectious diseases, peritonitis, etc., come into consideration.

Also in lumbar anesthesia a fall in blood pressure can probably be prevented through prophylactic dose of a pituitrin preparation.

Cure of Five Cases of Exfoliative Erythroderma. — Paul Unna, Jr. (*Dermatol. Wochenschr.*, 87 : 1317, 1928.)

In his method of treatment the author proceeded from the standpoint that it might be possible to remove most of the symptoms of the severe disease through easing the peripheral vascular system. He found support in the experiences which have been had with adrenalin treatment in acute toxic dermatoses (Salvarsan and mercury dermatosis). The principal value was placed on the unburdening of the heart and the influence on the peripheral skin vessels. The incisive action of adrenalin salve was especially shown in one case in which an attempt was made to reduce the adrenalin content of the preparation because of the high costs. The favorable action disappeared with the lowering of the adrenalin dosage and returned again with renewed increased use of adrenalin. The author is of the opinion that it will be possible to influence favorably most severe cases of pityriasis rubra Hebrae also through this adrenalin treatment. By this means a considerable advance might be obtained in a hitherto almost hopeless field.

Concerning the Surgery of the Parathyroids. — Westhues. (*Münch. med. Wochenschr.*, 75 : 1618, 1928.)

Transplantation of the parathyroids has little prospect of success. Blum's protective diet (without meat, rich in milk and hemokrin tablets) surpasses all former methods in activity. The author reports concerning several cases of parathyrogenous tetany and a case of the most severe exophthalmic goiter which could be influenced only by Blum's protective diet.

The Measures for Stimulating Peristalsis. — K. Vogel. (*Klin. Wochenschr.*, 7 : 1695, 1928.)

Preparations of the pituitary are recommended for sluggishness of the intestines. The same preparations are first used to induce contraction of the uterus, above all, in weak labor pains. The pituitary products belong to the hormones, therefore, to the substances which are formed in definite organs, frequently in the endocrine glands, reach the blood and lymph passages and excite special physiological processes in cells and tissue. These hormones act as regulators of the circulation as well as of the vegetative and cerebrospinal nervous apparatus and of the metabolism, as "self regulation of the living substance." Cholin, which acts characteristically even in very marked dilution, especially may be designated as genuine hormone of intestinal movement and of the smooth musculature. According to all reports medica-

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ments prepared from the pituitary seem, therefore, actually to exert a stimulating action on the intestine, especially in post-operative paralysis; however, according to Trendelenburg, all are not reliable.

Pituitary and Epilepsy. — E. Redlich. (*Fortschrit. Med.*, **46** : 1083, 1928.)

Even though epileptic attacks are not observed so frequently in pituitary disease as in diseases of other endocrine glands, as for instance the female sex organs, the thyroid and the suprarenals, yet a whole series of cases favor the opinion that definite relations exist between epilepsy and the pituitary and that this gland has an undoubted significance for the general pathology of epilepsy. Up to the present, we are not in a position to fix the exact limits of those forms of epilepsy in whose pathology the pituitary plays a dominant rôle. Consequently, at the present time we can not make any definite statements regarding the administration of pituitary preparations in epilepsy.

A Case of Quincke's Edema following Insulin. — A. Neumann. (*Wien. med. Wochenschr.*, **78** : 1363, 1928.)

The problem here is the appearance of Quincke's acute, local edema following an injection of insulin. To be sure, this phenomenon was not called forth by the insulin itself but by protein substances, the complete removal of which is desirable. Moreover, an individual supersensitiveness of the patient may have played a rôle.

Concerning Synthetic Ephedrin in Urticaria. — W. Fränkel. (*Med. Klin.*, **24** : 1773, 1928.)

The author had the opportunity to test ephedrin medication in a severe case of urticaria. The therapeutic effect obtained was an excellent one. The superiority of the synthetically prepared ephedrin over the more strongly acting adrenalin was also shown in this case, especially in the possibility of oral administration. Moreover, the lack of disagreeable secondary effects (which are frequent with adrenalin and also with ephedrin) was felt to be especially agreeable.

The Chemistry of the Hormone. — G. Barger. (*Ergebn. Physiol.*, **27** : 780, 1928.)

Barger gives a very successful review concerning the status of our chemical knowledge of the hormones at the present time. He begins with adrenalin and follows with thyroxin, the two sole hormones with which one can now work with chemical formula. Insulin follows, in which at least the crystalline state of the product has been reached through the works of Abel and his associates. Shorter paragraphs concerning the hormones of the posterior pituitary lobe and the anterior pituitary lobe, of the ovary, of the placenta and corpus luteum, of the parathyroid and concerning secretin follow. Finally, the blood-forming substance of the liver and the substances of doubtful hormone nature (such as gastrin, histamin, cholin, carnosin and spermin) are briefly described.

Concerning the Treatment of Diabetes Associated with Pulmonary Tuberculosis. — M. Labbé, R. Boulin and L. Justin-Besançon. (*Presse méd.*, **36** : 1618, Dec. 19, 1928.)

The authors recall that rapidly evolving bilateral tuberculosis is a frequent complication of diabetes, especially serious when it occurs in the course of diabetes with denutrition.

They report the case of two patients treated by bilateral pneumothorax. Both have been under treatment for the past 3 years for diabetes.

In the first case, the evolution of the tuberculosis has been followed since July, 1927. Treated by a right pneumothorax in October, 1927, the patient underwent a left pneumothorax in October, 1928. In the other patient, insufflation of the right side practiced in October of this year was followed 1 month later by insufflation of the left pleura. The authors direct attention to the excellent tolerance of the patient to bilateral pulmonary collapse.

The conclusions which the authors draw from these observations, though provisional, concern the evolution of the diabetes, their general condition, and the development of the tuberculosis.

From the viewpoint of the diabetes, the establishment of the symmetrical pneumothorax does not seem to have added elements of gaseous acidosis, to the acid intoxication arising from the diabetes. On the contrary, the increased acidosis connected with the installation of the tuberculosis was rather alleviated since the installation of the pneumothorax. The quantity of insulin necessary, however, to enable the patient to tolerate a

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restricted carbohydrate diet remains extremely high.

From the viewpoint of their general health, the effect of collapsotherapy is shown in arrest of the fall in weight in one of the patients and gain of 5 kg. in the other.

From the viewpoint of the tuberculosis the expectoration has ceased and fever has fallen.

Moreover, it must be remarked that no signs of cardiac failure have been noted in this patient outside of a transient tachycardia with very transient cyanosis in one of them at the time of the installation of the pneumothorax.

In the discussion, *M. Courcoux* stresses the good influence of pneumothorax on the tuberculosis and diabetes: even without insulin, diabetes may be seen to improve after a pneumothorax has been established if the diet is suitable. Inversely, if the diet is poorly followed, diabetes increases and the tuberculosis is observed to rapidly become aggravated.

M. Rist remarks that these two cases come to the support of the successes which may be obtained with bilateral pneumothorax. The intervention is serious but the fatal prognosis of tuberculosis associated with diabetes should not be forgotten. It is modified since the patients may be treated with insulin and pneumothorax.

M. Cernot has observed a case of diabetes associated with bilateral tuberculosis which occurred despite insulin treatment, where the results of pneumothorax were deplorable.

Spleen and Rickets. — A. Rémond, L. C. Soula and G. Cauquil. (*Bull. Acad. Méd.*, **100** : 825, 1928.)

Rickets does not always have to arise through lack of sterins, but can also be caused through an endocrine insufficiency of their elaboration. This elaboration is normally undertaken by the spleen and reticulo-endothelial system. In rickets this system is insufficient and can be made normal again through treatment with ultraviolet light and organotherapy by means of sterins.

Concerning the Female Sex Hormone. — Laqueur. (*Münch. med. Wochenschr.*, **76** : 177, 1929.)

The female sex hormone can be used in female, especially climacteric, obesity, for its therapeutic effect owing to its action on metabolism. The use of the ovarian hormone in prostate hypertrophy is rejected; on the

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other hand, its administration for the purpose of transient sterility is held disputable. With respect to the antimasculine influence it is stressed that this extends only to the testis. There can be no doubt of the specificity of the female sex hormone in regard to the action on definite systems only, as well as with regard to extraction from definite tissues. With regard to the storage of the female sex hormone, new, partly unexpected experiences are reported which render more difficult the experiment concerning the balance of the hormone, but on the other hand, open therapeutic perspectives.

Recent Investigations concerning Experimental Hermaphroditism and concerning the Antagonism of the Sex Glands. — A. Lipschütz. (*Pflügers Arch. ges. Physiol.*, **221** : 439, 1929.)

Ovary was implanted intrarenally into male guinea pigs with both testes intact. In 3 of 14 experiments the female hormonal effect occurred in the mammary apparatus in the sense of hyperfeminization; in 2 cases secretion of milk and colostrum was also present. The results contrast with all experiments up to the present and may not be attributed to technico-operative factors. The male sex characteristics remain normal in contrast to endocrine active ovaries. All experiments on the capability for reproduction of hermaphroditic males result positively. E. T. Engle (*Proc. Soc. Exp. Biol. and Med.*, **25** : 715, 1928) reports concerning experiments in which he was able to promote the occurrence of female hormonal effects in rats with intratesticular ovarian transplantation by administration of the hormone of the anterior pituitary.

The Reactions of the Organism in the Eczemas. Sensitization Syndrome. — H. Jausion and P. Cot. (*Paris méd.*, **19** : 67, 1929.)

The functional involvement of the endocrine glands in the symptom picture of eczema has been repeatedly demonstrated yet no general rule could be established in these individual findings. H. Vincent assumed a dysfunction of the thyroid as cause of the Malpighi spongiosa; many authors were able to observe a relationship between the onset of eczematous symptoms and the function of the ovary. J. Meyer and Gallerand on the contrary obtained undoubted results through the injection of testis extract in women without wishing to assume for this reason a causal relationship with respect to the etiology of the disease and the result. The common embryonal origin of the vegetative and endocrine system explains their synergism. It has been established that the suprarenals regulate the sympathetic tonus and maintain it. What the hormone of the suprarenal effects may be attained by the therapist only in very limited degree through adrenalin; this characterizes the circle of action of the thyroid hormone also. Garrelon, Santenoise and Legrain demonstrated the double function of insulin, which on the one hand regulates the nature of pancreas secretion and on the other, through maintenance of the vagal tonus, acts on a vagotonizing hormone whose secretion it activates. In this way, an explanation for the fluctuations of glycemia in sensitized individuals would also be given. All these findings and considerations demonstrate the significance of the endocrino-vegetative system.

Edema and Edema Formation. — O. Jervell. (*Tidsskr. norske Laegeforening*, **49** : 73, 1929.)

Pernicious anemia is one of the diseases in which a tendency to edema exists. These edemas resemble the nephrotic to a certain degree in their localization. The finding is characteristic that these edemas arise in the periods of exacerbation of the disease and disappear under liver treatment with remission. As cause of the readiness for edema in diabetic patients a certain undernutrition must be assumed as etiological factor. Especially in patients who receive sodium bicarbonate, this tendency to formation of edema is to be observed. This question receives a special interest at the present time through the edema frequently appearing during insulin treatment. Insulin edemas are most frequently observed in patients who have previously been in precomatose or comatose state. The size of the dose of insulin administered as well as the water and salt content of the diet seem to play a rôle in this. Petren and Odin regard the alkalosis called forth by insulin as the most important cause of water retention. O. Klein assumes changes of blood viscosity through the action of insulin; Vollmer and Serebriski refer to the antagonistic relation between pituitrin and insulin; other authors bring into consideration the action o

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insulin in influencing the amounts of globulin and fibrin in the plasma. The author believes that the formation of edema which is observed during insulin treatment, is to be attributed to changes of the colloid-osmotic pressure of the blood. The possibility is also to be drawn into consideration that the permeability of the capillary is changed in diabetics.

Concerning Female Sex Hormone. — M. Kochmann. (*Würzburger Abhandl. Gesamtgeb. Med.*, 5 : 173, 1928.)

De Veer has obtained from whole ovary as well as from corpus luteum with the aid of organic solvents an extract which influences the metabolism of female animals in a particular manner. In acute experiments of several hours, following injection of this extract, the oxygen consumption rises, whereas the CO_2 excretion increases in the same measure. The respiratory quotient is markedly lowered. Male, sexually mature animals do not show this influence, in contrast to young, sexually immature and castrated animals. Kochmann and Wagner believe from their similar results that they have a new hormonal substance specific for female animals, which they call Oobolin. It is not identical with the menstruation hormone.

Nuernberger used Oobolin in a small number of cases and observed two to three strikingly favorable results in addition to failures or doubtful results. Whether other hormones are also present in Oobolin or whether the estrus hormone also present in Oobolin comes into action the author is unable to say. According to the experience of Hartwich, Kochmann believes that Oobolin might also be indicated in adiposity of ovarian origin.

Organotherapeutic Treatment of the Symptoms of Obesity, Sterility and Migraine in Ovarian Insufficiency. — A. Ulrich-Lévy. (*Progrès méd.*, No. 9 : 380, Mar. 2, 1929.)

Independent of the genital and menstrual disorders which are proper to it, ovarian insufficiency includes a very frequent symptomatic triad: obesity, periodic headaches and sterility. The treatment capable of influencing these three cardinal symptoms effectively may be considered as acting energetically on the ovary itself. Such a treatment should evidently attempt to be pathogenic and should take into consideration the cause of the insufficiency. The classical emmenagogues are of but little assistance. Organotherapeutic treatment is much more logical and causal.

With ovarian extracts and especially with dissociated ovarian therapy (corpus luteum and ovary without corpus luteum), success is frequently obtained. The author has frequently noted the cure of simple ovarian insufficiency particularly in young girls by this method.

In the presence of an adiposogenital syndrome, however, when the obesity occupies a preponderant place, the author prefers the use of spermatogenetic organotherapy. The results which spermatogenetic therapy has given, administered, according to the case, either in injections or orally, are illustrated by six cases reported.

While the author considers that there is indication for ovarian organotherapy in the presence of a hypo-ovarian syndrome, she believes that in certain cases it is preferable to give spermatogenetic organotherapy if obesity, sympathetic disorders with or without psychic disturbances and sterility predominate.

It is of course understood that such a treatment does not exclude any of the adjuvant medications, physical, hydrotherapeutic, gymnastic, etc. Thus, in certain cases thyroid or euthyroid serum has been added to the spermatogenetic extract in order to obtain the maximum therapeutic effect. Thyroid extract and spermatogenetic extract were never used simultaneously, however, as their similarity of action is great enough to contraindicate their use at the same time.

Clinical Contribution to the Question of the Atrophoderma. — O. Blatt. (*Dermatol. Wochenschr.*, 88 : 190, 1929.)

The assumption of the endocrino-sympathetic genesis of this skin process seems to have taken firm ground. The author assumes the common pathogenic factor for this group of skin disorders in the endocrine system. On the basis of clinical observations, acute and chronic infections are regarded as exciting causes (syphilis). Among 38 cases the author found hypofunction of the pituitary in 15 cases, hypofunction of the ovary in 13 cases, hypofunction of the thyroid in 5 cases, hypofunction of the suprarenals in 3 cases, hyperfunction of the suprarenals in 3 cases, hyperfunction of the thyroid in 6 cases, normal function of the thyroid in 5 cases, normal

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function of the ovary in 3 cases, normal function of the suprarenals in 10 cases, normal function of the pituitary in 1 case.

On the Subject of Dermatofibrosis Lenticularis Disseminata. — A. and L. Pokorny. (*Dermatol. Wochenschr.*, **88** : 157, 1929.)

The authors stress the circumstance that the hitherto known four cases concerned women only and that the three cases of personal observation showed internal secretory disorders and relations could be discerned between dermatofibrosis lenticularis disseminata and the ovarian function. In the one woman the dermatosis appeared with the beginning of the menopause; in the younger daughter of this woman the relation of disturbed ovarian activity was still more definite; in the third patient, the older daughter, a polyglandular disorder seemed to be present. In this patient there also exists a certain adiposity which together with the delayed growth in length may be attributed to the small thyroid.

The Action of Posterior Pituitary Preparations on the Intestine

(*Continued from page 329*)

"5. Papaverine antagonizes the morphine action in both types of segments."

There would seem to be no doubt that solutions of post pituitary contain a substance or substances that exert a specific action on the smooth unstriped muscle of the intestine. Histamin and cholin are apparently excluded. The effect is dependent upon the concentration and existing tonus. Both the pressor and oxytocic fractions of pituitary solution give this effect. Clinically it appears to be of value, injected hypodermically, in intestinal paralysis.

1. Shamoff, V. N., *Am. J. Physiol.*, 39 : 268, Jan., 1916.
2. Hoskins, R. G., *J. Am. Med. Assn.*, 66 : 733, 1916.
3. Gruber, C. M., and Robinson, P. I., *J. Pharmacol. and Exp. Therap.*, 36 : 203, June, 1929.
4. Gaddum, J. H., *J. Physiol.*, 65 : 434, Aug. 14, 1928.
5. Gruber, C. M., and Pipkin, G., *J. Pharmacol. and Exp. Therapy.*, 38 : 401, Apr., 1930.

Embolism and Cardiac Syncope Ten Days after a Laparotomy; Intracardiac Injection of Adrenalin. Recovery. — Lutaud. (*Presse méd.*, **37** : 7, 1929.)

Ten days after an appendectomy and hysteropexy a patient suffered from a severe collapse following embolism. The author injected 2 cc. of a solution of adrenalin (1:1000) into the heart after the patient's heart had been stilled for somewhat less than 10 minutes. The woman was not merely momentaneously resuscitated but complete recovery was effected.

Lesions Found at Autopsy on a Subject Affected by Adiposogenital Syndrome. — Babonneix and Lhermitte. (*Presse méd.*, **37** : 408, Mar. 27, 1929.)

The patient had suffered from hydrocephalus with hydromyelia and an adiposogenital syndrome with polyuria. At autopsy, in addition to the hydromyelia, they found a very marked hydrocephalus with atrophy of the tuber; they established a relation of cause and effect between these lesions and the syndrome.

Tuberculous Ovarian Semi-Sclerosis — New Endocrine Syndrome. Its Treatment. — M. Laemmer. (*Presse méd.*, **37** : 8, 1929.)

The symptoms of the disease form described are: dysmenorrhea or amenorrhea, toxic gain in weight; similar to the forms in hypofunction of the thyroid where the thyroid, however, plays no rôle; traces of signs of a tuberculous disease, decalcification and dephosphatization (urine analysis); change in blood pressure; small, hard ovaries.

Thyroid therapy is quite ineffective. Treatment with corpus luteum or ovarian therapy alone is without result. The following plan is much more necessary: injections of follicullin every second day, diathermia, dietetic, antituberculous treatment, phosphate, calcium.

Inquiry concerning the Cause and Treatment of Chronic Joint Diseases. Introductory Paper. — A. Laqueur. (*Med. Klin.*, **25** : 137, 1929.)

Among other questions, Laqueur asked (1) what part falls to hormonal causes in chronic joint diseases, according to the experience of his colleagues present at the meeting? (2)

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As in recognition of this cause, is the percentage portion of primary chronic joint rheumatism (polyarthritis chronica progressiva) in the female sex to be supposed to be considerably greater than the percentage portion of infectious arthritis and of genuine arthritis deformans? (3) What therapeutic consequences does the meeting draw from these experiences?

H. Schlesinger, p. 138: Hormonal factors might play only a modest rôle in the origin of chronic arthritis, if one disregards Heberden's nodules. Schlesinger did not observe convincing results of hormonal therapy.

J. Breemenvan, p. 138: Among the female patients in the polyclinic suffering from arthritis, a great number of the diseases are in all probability to be related to hormonal disturbances. The author believes that hormonal therapy is used with success in various cases. Thyroidin is especially effective in these cases. Other preparations like Hormotone, etc., have occasionally given favorable results.

S. Morawitz, p. 139: Hormonal factors at least play a decidedly significant rôle as supporting factor in the form of polyarthritis chronica rheumatica which appears in women for the first time in the climacteric or increases at this time. Whether such hormonal disorders are able to cause polyarthritis chronica by themselves alone, Morawitz is unable to decide. Hormonal therapy was never successful in the cases of the author.

P. Köhler, p. 140: Hormonal influences are of course of great significance; the ovaries especially play a great rôle in the disease picture of so-called primary chronic joint rheumatism; still Köhler does not believe that there is an independent disease, which is only conditioned through ovarian glands. The hormones act through the influencing of mineral metabolism, of the autonomic nervous system, of the alteration of metabolism of the tissues so that the ground is prepared for arthrotropic damage. A hormonal therapy is important as adjuvant and direct influence on the supporting tissue or indirect, for example, in thyrogenous obesity. The author has not observed a cure of primary, chronic joint rheumatism; on the other hand, administration of hormonal preparations seems to have a favorable action on the course.

S. Krebs, p. 140: It should be unquestionable that hormonal causes play an etiological rôle in chronic arthritis, especially in women. Hormonal therapy has brought to light very few uniform results in chronic arthritis of presumably endocrine origin.

Concerning the Influence of Insulin on the Liver. — E. Forsgren. (*Acta med. scand.*, **70** : 139, 1929.)

From the author's experiments it may be seen: that insulin exerts no noticeable action on the glycogen content of the liver and does not affect the rhythmic activity of the liver.

The susceptibility for insulin seems to vary with the rhythmic activity of the liver and to be greatest in the secretory phase when the glycogen content is low.

Practical Therapeutics

(*Continued from page 342*)

ism, such a delicate and nicely balanced mechanism as the central nervous system can not help but be involved. Whether this is what actually does take place, or whether the endocrine dystrophy and the changes in the central nervous system are, alike, the result of some more obscure etiology, possibly of a genetic nature, is yet to be proved. That certain parallels of this character do occur is evident, and there is ample experimental evidence to warrant the belief that changes in the glands alone are adequate to bring them about. The studies of Lipschütz, Moore, Myers, Sand and others upon the male sex-glands following castration and vasectomy prove beyond question the power which these glands, at least, have in influencing psychic development and change. Other equally convincing evidence has been submitted by Cushing, Dercum, Kanavel, Goetsch and others as regards the pituitary, while the psychic relationship of thyroid and pancreas has become well known.

While it is quite true that our knowledge of symptom-complexes is not yet adequate to enable us to definitely fix upon the exact gland or glands involved in many cases, yet it is equally true that while a single gland may be primarily involved in many instances, these manifestations are invariably to be attributed to a derangement in varying degree and proportion, of the whole endocrine system.

Affections of the female sex glands unquestionably have extremely far-reaching and important psychic effects. The high rate of mental disturbances coincident with the onset

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of puberty and with the climacteric is in itself evidence of this, as are the disturbances so often found following castration in the female. The exact relationship existing between the ovaries and mental deficiencies is not clear.

In a summary Downs concludes his paper as follows:

A majority of the endocrine dystrophies present marked and definite psychic symptoms peculiar to their class. It seems probable that both somatic and psychic symptom-complexes are the result of endocrine disturbances, acting upon the entire organism, including also the other glands of internal secretion. It is probable that still deeper than these hormone effects are other more obscure causative factors, which, through the glands of internal secretion, affect the entire organism. It is obvious that the way in which experimentally produced endocrine variations affect the organism is a close parallel to many definitely hereditary aberrations. It seems, then, plausible to believe that heredity may in great part function through the medium of the endocrine system, to produce definite symptom-complexes involving both physical and psychic changes of definite and characteristic types.

Chronic Mental Disease Associated with Ovarian Dysfunction. — Alfred Danby and Kathleen Sykes. (*Lancet*, **216** : 129, Jan. 19, 1929.)

Within recent years a considerable amount of attention has been directed to the organic factor in the etiology of mental disease. In this connection a case is reported the outstanding features of which were the remarkable exacerbations of mental symptoms at a particular phase of the menstrual cycle, and their complete remission after resection of the diseased part of the ovaries.

The irregularity of the menstrual process in interval, duration, and amount was a clear manifestation of disordered ovarian function; the pathological findings were in accord with this.

In view of the present work on estrin, and the apparent physiological antagonism between the estrus-producing hormone and that of the corpus luteum, it seems reasonable to infer that the morbid condition of the ovaries had interfered with the normal correlation of their cyclic functions. Presumably this derangement had thrown out of gear the endocrine balance which, in this instance, had caused a psycho-pathological reaction.

Achondroplasia and Pure Dwarfism. — Patel and Carcassonne. (*Presse méd.*, 37 394, Mar. 23, 1929.)

The authors report the case of two dwarf whom they had occasion to treat for surgica affections. One is a subject of 1 m. 37, pre senting the deformities characteristic of achon droplasia of the rhizomelic type of Pierre Marie, as shown by measurements and th general appearance of the patient with hi powerful musculature on the bones of th shortened members, his large head and hi adult's body. Radiography reveals the clas sical deformities: The sphenoidal and fronta sinuses are enormous; the bones of the mem bers have large exostoses. Mentality i normal.

Contrasting with the first patient, th second is a dwarf of very different type. man of 1 m. 42, the bones of whose member body and head are small and feeble. It is question of purely congenital dwarfism in th patient; there is no infectious history, n cardiac lesion suggesting dwarfism of infantil type (Lorain's type). The thyroid body i normal and the appearance of a miniatur man is entirely different from the Brissau type of dwarf or the myxedematous.

Functional Hemorrhages in Gyne cology. — M. Henkel. (*Med. Klin.*, 25 60, 1929.)

Calcium enrichment of the blood, adminis tration of iron and nourishing food are ver important in the therapy of function gynecologic hemorrhages. That organ therapy plays a large rôle is evident. It mus however, be made clear that several inje tions of a properly chosen hormone can n "effect a cure." This will only be the cas when the endocrine deficiency is not onl transiently but permanently compensate by functional regulation of the organ an that can take a long time.

Pituitary — Midbrain System and Fa Metabolism. — W. Raab. (*Wien. klin Wochenschr.*, **42** : 238, 1929.)

Discussion of the action of pituitrin in fa metabolism. In the dog, pituitrin causes regular, characteristic effect attained throug no other hormone preparation. To attain this pituitrin effect probably very large doses ar required in the dog with subcutaneous inje tion, whereas with injection into the brai

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ventricle small portions of it suffice. This behavior shows the correctness of Biedl's assumption that pituitrin acts in the vegetative metabolic center of the midbrain. Following destruction of the tuber cinereum the pituitrin effect remains absent, just as following poisoning with drugs which act in the midbrain: pyramidon, antipyrin, etc.

The conclusion is reached that pituitrin furthers the absorption of fat from the blood on the part of the liver by the above described nerve route and the destruction of this amount of fat in the liver. Numerous clinical and anatomical observations have established the appearance of obesity following lesions of the pituitary alone as well as of the vegetative centers alone and of both at the same time.

T. C. Hunt, of course, missed each effect in obese individuals following several injections of pituitrin (1 cc. daily for 6 to 13 days) in fact small increases in weight even occurred. Nevertheless, the fact of a specific influence of pituitrin on fat metabolism is established on the basis of extensive uniformly positive experimental series.

Concerning the Action of Very Small Doses of Thyroxin on Gas Exchange of Invertebrates. — Romeis and Wüst. (*Naturwissenschaften*, **17** : 104, 1929.)

In investigations concerning the action of mammal hormones on invertebrates, the influence of thyroxin on oxygen consumption of butterfly chrysalis was also tested and an average rise of oxygen consumption of about 30 to 50 per cent was found.

New Methods of Treatment of Exophthalmic Goiter. — B. Aschner. (*Hippokrates*, **1** : 366, 1929.)

Failure is frequent in the treatment of many cases of exophthalmic goiter. Iodin, ovarian tablets and antithyroidin are given and a sensitive stomach is overloaded (which contributes very much to the aggravation of the total symptoms).

The further important factor in the constitutional treatment of exophthalmic goiter is the behavior of the menstrual function. In too weak or infrequent menstruation, ovarian preparations in the form of tablets or injections may be given. Several cases of improvement have actually been observed following ovarian therapy. It must, however, be recalled that ovarian tablets frequently irritate a sensitive stomach very much and may make an existing dyspepsia worse. Ovarian injections bring substances alien to the blood into the circulation and in this way increase the existing autointoxication. The author accordingly prefers emmenagogues.

The skill of the physician consists not merely in using as purely mechanical measure in each patient a few specific remedies such as Basedow-antithyroidin, but in giving each individual case individual attention, as do the homeopaths in their field.

Indications for a Conservative Therapy of Glaucoma. — R. Thiel. (*Therap. Gegenw.*, **70** : 71, 1929.)

Very narrow limits are drawn for the therapeutic use of adrenalin in this complaint. As contraindication are above all to be considered: diabetes mellitus, exophthalmic goiter, severe degenerative changes of the heart and blood vessels. The point of attack of adrenalin in the eye appears to lie exclusively in the vessels according to clinical experiences made thus far. If these are damaged to such an extent that the expansion of the wall as well as the permeability are irreparably disturbed, adrenalin is no longer active. Moreover, a maximum midriasis is occasioned by adrenalin before the desired contraction of the intraocular vessels has appeared in the depths; this midriasis, however, signifies an essential danger for the eye. Adrenalin treatment is most active in acute iritis with rise of pressure and can also be of value in glaucoma simplex. The use of adrenalin is not to be recommended in absolute or hemorrhagic glaucoma.

The Cachexia of Growth, Pluriglandular Syndrome with Pancreatic Participation. Favorable Action of Insulin. — E. May and F. Layani. (*Bull. et mém. Soc. méd. Hôp. Paris*, **45** : 302, Mar. 4, 1929.)

A young girl of 16 years shortly after the establishment of menstruation presented an increase of growth, accompanied by various disturbances, vasomotor manifestations, then a disappearance of menstruation and finally a considerable loss of weight. At the same time there was a slowing up of nutrition as shown by the low basal metabolism.

These disorders are of interest in their grouping and their intensity. They furnish an exaggerated picture of the findings observed in young people of both sexes at the time when they are growing and when sexual

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function is established. In general, however, all these disturbances attain only moderate intensity. In the present case the intensity of the manifestations of growth was sufficient to cause hospitalization. The emaciation especially was actually impressive and justified the name of cachexia of growth. The appearance of this disorder at the time of puberty tended to incriminate endocrine disturbance and the pronounced emaciation suggested the idea of pituitary cachexia. The ovary also played a rôle in this case as shown by the arrest of menstruation and the exaggeration of the cyanosis of the extremities. Moreover, the great fall of basal metabolism hardly ever exists at such a low state without a weakening of the thyroid function. Finally, the action of insulin on emaciation suggests a pancreatic deficiency. The cachexia of growth accordingly appears to be essentially a pluriglandular syndrome. At the time of life when the child is transformed into the adult it requires a common effort of all the endocrine glands. In certain subjects probably presenting a congenital or acquired glandular debility, the endocrine apparatus is unable to furnish this effort and gives signs of failure. In this pluriglandular syndrome a part should be given to insufficiency of the endocrine pancreas. In this patient the pancreatic deficiency was manifested by a considerable emaciation but without diabetes.

Treatment gave very interesting results which showed to what extent the various endocrine glands in the true pluriglandular syndromes may remain independent of one another despite the common signs of deficiency. The action of insulin was striking on the emaciation but on this symptom alone. With 10 units of insulin daily for 6 weeks, the patient regained 15 kilograms between the beginning of June and the middle of September and this gain in weight continued more slowly after cessation of the insulin therapy. On the other hand, menstruation did not return and basal metabolism remained as low as at the beginning of the treatment. Only after another specific therapeutic treatment, thyroid and ovarian, did the metabolism again become normal and was menstruation reestablished. Thus, the pluriglandular deficiency reacted only to its particular stimulus and the authors believe it well worth while to direct attention to this independence of the various elements of the pluriglandular syndrome. They were especially surprised to observe great emaciation coinciding with a fall of basal metabolism. It is difficult to understand how an improvement in assimilation as shown by a gain of 18 kgm. should not be accompanied by a parallel modification of the basal metabolism. It must then be admitted that the relations which unite basal metabolism and the activity of the nutrition are more complex than one would think at first glance.

The authors' observation also shows what favorable results may be obtained in states of difficult growth and denutrition of puberty.

William Stokes

(*Continued from page 345*)

were nights of entertainment with music in which Stokes himself was well informed, as well as an accomplished player; there were also discussions in art with Petrie, and timely topics of the world in general. (It was at one of these gatherings that Carlyle met Stokes.) Stokes was no politician; he did not care to mix in the affairs of "Young Ireland," yet he did not cease to be a patriot. He states, on the contrary, "To me the real patriot is he who, in a life of labour and of trial, with integrity, practical wisdom, and far-seeing intelligence, labours onward to no other end but that his country shall rise, and with the honourable and justifiable ambition that, loving her, he may rise with her also."

For all his energetic nature and brilliant career Stokes remained a benevolent, charitable person, always seeking thoughtfully and wisely to alleviate the pain of the sick and bereaved, not only in his work but also in his home. Sir Henry Acland says of him that he combined "real delight in all intellectual development with the deepest sympathy for suffering." He was universally acclaimed by men of his profession as well as by those whom he treated in the clinics, by his associates and by his well-loved family. The closing years of his life were saddened by the disintegration of his family circle through sickness and death. After the loss of his wife his interest in living seemed to wane, his energy and vitality decreased so that he was incapable of pursuing the industrious method of work he had enjoyed previously. One day, in stepping from a carriage Stokes suffered a fall which ultimately caused his death (January 6, 1878) from a paralytic seizure.

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Investigations concerning Elective Nutrition and Growth. — H. Reiter. (*Med. Klin.*, **25** : 268, 1929.)

In the investigations undertaken it was a question of clearing up metabolic processes, which are closely connected with a feeding of elective food complexes; in particular the influence of administration of certain food mixture on growth should be more closely investigated. As food substances added to the diet, liver substance and beef testis substance were chosen. The latter was at the same time observed for the presence of a sex specific action through enteral administration. Investigation was also made whether this addition to the diet succeeds in again completely removing the disease picture induced in animals by the Stepp diet.

In the investigations undertaken it could be shown that liver substance, relatively sparing, freed from moisture and not to be considered as denatured, as well as testis substance treated in the same way, not only supplies the deficiency of the Stepp diet but even as a rule very rapidly and completely alleviates the injurious effect of the Stepp diet. The intensity of growth is extraordinarily strongly favored by administration of non-denatured substances, and leads to considerable weight values in male animals, under the use of testis substance. The intensity of growth corresponds to the value of the hemoglobin content and the erythrocyte count.

Concerning the Delay in Consolidation of Fractures Due to Syphilis (Unknown). — L. Bory. (*Progrès méd.*, **56** : 343, 1929.)

In a 25 year old patient a fracture of the leg failed to consolidate within 9 months. When syphilis was noted on the basis of a positive Wassermann reaction, a specific treatment was first given and later a general treatment with organotherapy. The patient received a calcium preparation in which a thymus powder (0.20 gm.) and a parathyroid powder (0.30 gm.) were combined. After 7 weeks, the complete consolidation was demonstrable clinically as well as radiologically.

Diabetes and Exophthalmic Goiter Associated. — M. Labbé and Gilbert-Dreyfus. (*Paris méd.*, **19** : 429, May 4, 1929.)

Diabetes mellitus is so frequently found associated with exophthalmic goiter in the clinic that we can not speak of a simple coincidence but must admit an actual morbid relation. Moreover, the constant disorder of glycoregulation revealed by the test of hyperglycemia in exophthalmic goiter shows that thyroid hyperactivity exercises an influence on the metabolism of sugars. The frequency of this association is not very great. The goiter is most frequently the first to appear and diabetes takes second place. Sometimes, however, it is the diabetes which occurs first. According to statistics, of Joslin and Lahey and Wilder, it is the toxic adenomatous or secondarily basedowified goiter which is most often accompanied by diabetes. Primary exophthalmic goiter is a little less frequently responsible. The observations resemble each other sufficiently to characterize a special clinical type. When the pathological picture is complete, it is that of an intense exophthalmic goiter in which the basal metabolism reaches a high level, higher on the average than that of isolated exophthalmic goiters, according to Joslin.

The diabetes may show all the degrees of severity: at times benign, representing a thyroid glycosuria rather than a true diabetes, at times diabetes without a nitrogenous denutrition, of moderate intensity, at times severe diabetes with nitrogen denutrition and acidosis.

Death is most often due to coma. It is generally an ordinary acidotic coma, at times it is a state of cardiac collapse associated with acidosis. This was the case in the observation reported. In the majority of cases the diabetes and the exophthalmic goiter evolve together, undergoing simultaneous exacerbations. This is not observed in all cases.

The frequency of association of diabetes with exophthalmic goiter, the evolution by simultaneous exacerbations of the two diseases suggested to M. Labbé that there might be a thyroid diabetes under the jurisdiction of a special pathogenic mechanism distinct from that of the usual pancreatic type of diabetes. In thyroid diabetes disturbances of glycoregulation would be due to hyperthyroidism whereas in pancreatic diabetes it is due to insufficiency of the insulin secretion. We know that the glycoregulative function is complex and that various organs participate in it. Among these the pancreas and the thyroid play an antagonistic rôle. Numerous animal experiments and clinical observations on exophthalmic goiter patients unite in bringing to light the rôle of hyperthyroidism

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in the pathogenesis of glycoregulative disorder. These experiments tend to show that hyperthyroidism may create a true diabetes in which the liver has become incapable of retaining glycogen just as in ordinary diabetes where insufficiency of insulin has likewise abolished the glycogenic function. This thyroid diabetes must follow the same evolution as exophthalmic goiter.

All the authors admit that active treatment of the exophthalmic goiter with iodin, x-rays, thyroidectomy simultaneously exerts a favorable action on the associated diabetes. This action is however not always easy to show. The authors report a case in point in which iodin on two occasions had a very definite moderating effect on the exophthalmic goiter; diet and insulin acted very effectively on the diabetes; insulin had no action whatever on the goiter; iodin (after having improved the goiter) did not seem to simultaneously ameliorate the diabetes at the beginning but contributed to its improvement in a later phase.

The demonstration of the improvement of diabetes by the intervention of improvement of exophthalmic goiter by iodin treatment is not as definite as could be expected and the experiment should be undertaken again. Nevertheless it seems that the diabetes while reacting distinctly to diet and insulin was also influenced by antithyroid medication and behaved like a thyroid diabetes. In the presence of these facts we arrive at a less simple conception of diabetes in exophthalmic goiter patients than before.

Basedowian diabetes is fundamentally an ordinary diabetes due to insufficiency of the internal secretion of the pancreas like all diabetes; it reacts to diet and insulin like all the diabetes. Yet it is distinct from ordinary pancreatic diabetes because it evolves simultaneously with exophthalmic goiter and because it is at times less definitely sensitive to the action of diet and insulin. In reality its pathogenesis is complex. The disorders of glycogenic function result here not only from insulin insufficiency but also from excess of secretion of thyroxin. Hyperthyroidism which would not itself be capable of creating a severe diabetes may very easily aggravate a moderate diabetes associated with intense pancreatic insufficiency. It lowers the capacity for utilization of carbohydrate, it produces nitrogen denutrition, it excites acidosis; finally, it may render the subject relatively less sensitive to the action of diet and insulin.

Thus, pancreatic hypo-insulinism and thyroid hypersecretion add their effects to produce a diabetes of serious type. At the same time the treatment of this diabetes demands the cure of the exophthalmic goiter at the same time as diet and insulin therapy. The cure of the exophthalmic goiter improved the diabetes but did not suppress it.

It remains to learn why diabetes is more frequent in exophthalmic goiter patients than in ordinary subjects. Is it because the hyperthyroidism reveals a moderate insulin diabetes which without it would have remained latent? Is it not rather because of a coincidence rather frequent in affections of the various endocrine glands, an endocrine synergism? In any case, these endocrine interrelations were interesting to study to understand the pathogenesis and clinical evolution of the diabetes associated with exophthalmic goiter and to arrive at a curative therapeutic method.

Experimental Researches on the Corpus Luteum. — L. Brouha and H. Simonnet. (*Presse méd.*, **37** : 591, May 4, 1929.)

Injected into normal female rats, extracts of corpus luteum permit the suppression of the estrous cycles if the dose is sufficient. The genital tract then assumes an aspect analogous to that found in the castrated animal. With smaller doses there is created a state recalling pseudo pregnancy with characteristic estrus but with development of the uterus. With very small doses there is simply prolongation of the interestral periods.

In the immature animal the extracts retard the appearance of the first estrus. In the castrated animal they do not provoke any development either of the uterus or of the mammary gland. The extracts act on the estral phenomena probably by suppressing the production of folliculin and not its action, for, if we inject folliculin and extract of corpus luteum simultaneously, the latter does not prevent the effects of folliculin from showing themselves.

Anterior Pituitary Hormone and Male Genital Tract. — L. Brouha and H. Simonnet. (*Presse méd.*, **37** : 591, May 4, 1929.)

Daily intramuscular implantation of fragments of anterior lobe of pituitary shows that this gland exerts a marked stimulating action on the male genital tract (rats, mice). The action of anterior pituitary extracts varies

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with the method of preparation and sometimes with the dose used. In utilizing the active principle contained in the urine of a woman at the beginning of pregnancy, there is regularly observed an enormous development of the genital tract in the immature animal and in the adult.

With anterior pituitary extracts prepared by alkalin route, a certain development is obtained with small doses; on the contrary, with large doses an arrest or regression. It is not yet known whether these effects are due to two antagonistic substances or to a single substance acting differently according to dose injected.

Concerning the Action of Kidney Extracts. — E. Freund. (*Wien. klin. Wochenschr.*, **42** : 696, 1929.)

The study of the chemical function of most organs has remained a very limited one. The author has already drawn attention to the fact that it might be the task of organotherapy to extract the active substances in all organs and above all in the kidneys and to test them for their therapeutic action.

Concerning the Weakening of the Toxicity of Adrenalin by Some Organic Substances. — G. Boivin. (*Paris méd.*, **19** : 520, 1929.)

The author studied the mechanism of the lowering of the toxicity of adrenalin through aqueous alcoholic extracts of organs. He criticizes the use of a pancreas extract for this type of investigation, since his own studies showed him that the majority of the other organs possesses the same action, and stronger than pancreas extract, if they are injected into rabbits at the same time as the adrenalin. As regards the protective action of a pancreas extract injection in acute pulmonary edema, this is not constant. From the therapeutic standpoint this does not appear to have any interest.

A Case of Exophthalmic Goiter Refractory to Insulin. — W. Kreiner. (*Deut. Zeitschr. Chir.*, **216** : 285, 1929.)

Report concerning a patient with exophthalmic goiter which is noteworthy because of refractory behavior to insulin with simultaneous excretion of sugar. Following removal of the purely parenchymatous goiter, recovery of the patient occurred with no excretion of sugar.

Dependence of Vagus Tonus on Adrenalinemia. — G. Viale. (*Klin. Wochenschr.*, **8** : 73, 1929.)

A number of harmonious experiments have led the author to make the assertion that the tonus of the heart vagus is dependent on the amount of adrenalin circulating in the blood, and that the acceleration of the pulse which is normally to be observed following division of both vagi, is not dependent upon the suppression of an autochthonous tonus of the vagus centers but initially upon an increased secretion of adrenalin, later upon a sensitization of the heart under the influence of the vagi to the adrenalin.

Experiments undertaken by the author led him to the conception that the vagus tonus represents less an autonomic condition of the corresponding centers than the action of adrenalin on these. If adrenalin is deviated, the vagus tonus also comes to nothing. That adrenalin also possesses a vagal action has recently been stated by Smirnow as well.

The vagus tonus which in general is regarded as the expression of the autochthonous activity of the corresponding nerve centers is dependent upon the lasting presence of adrenalin in the circulating blood.

Remarks Concerning Niehans: "Endocrine Glands and the Methods of Rejuvenation." — Enderlen. (*Schweiz. med. Wochenschr.*, **59** : 264, 1929.)

In transplantations of glands executed by him, the author observed necrosis of the transplant in all cases.

Local Anesthetics and Suprarenin. — Eduard Rentz. (*Arch. exp. Path. u. Pharmakol.*, **144** : 310, 1929.)

Tests on the effective capacity of suprarenin in conjunction with members of the cocaine group, gave the following information. The effect of suprarenin, 1:10 millions, is increased by cocaine derivatives. The constricting effect on the blood vessels is not intensified by suprarenin in slight concentration, rather this furthers the vasodilating effect of the cocaine after the initial constriction. With the administration of suprarenin in stronger concentrations, the antagonism of several cocaine derivatives was overcome, partly, and the suprarenin effect, even if decreased, lasted for days. By means of cocaine, novocaine, alypin, and psicaine the effect of suprarenin was inhibited or increased, but not greatly reversed.

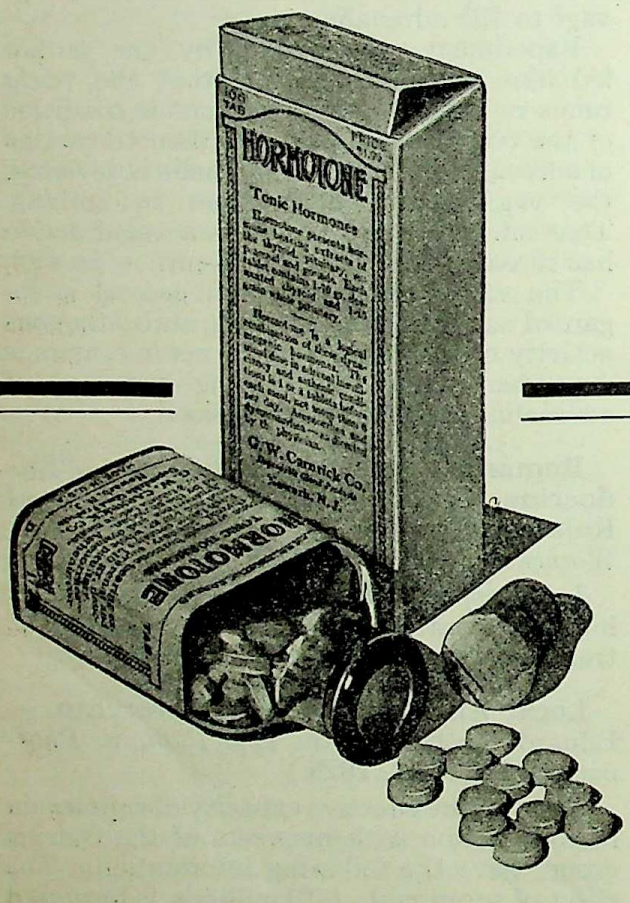
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EQUALIZE THE SUPPLY OF INTERNAL SECRETIONS AT THE MENOPAUSE

"Of what does the 'endocrine crisis of the menopause' consist? Or in other words what glandular elements usually take part in it? I believe these three, the genital, the thyroid and suprarenal are the fundamental elements entering into the development of the crisis."

(Gregorio Marañón, *The Climacteric,* 1929.)



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Clinical Contributions on Diseases of Metabolism. II. Corpulency and Obesity. — P. F. Richter. (*Deut. med. Wochenschr.*, **55** : 1575, 1929.)

Gland preparations are very important, above all thyroid gland preparations, in the accomplishment of modern therapy of obesity. There are, besides, cases of extensive "corpulency" in which, however, a certain endogenous storage and deficient adaptability of the thyroid gland function and therewith of the oxidation of the over-nutrition, are quite commonly evident.

If the diabetic preparations do not act effectively in these instances, the therapy may be supplemented by thyroid dosage without hesitation, naturally under certain precautions. These are large dosage (0.1 per dose to 0.3 per day) and avoidance of a treatment of long duration (not over 4 weeks), no strict dietary restrictions and finally interception of the thyroid treatment with the occurrence of weakened condition of the heart. One can fare as well as ever with oral administration. Rather rigorous limitations are thus placed on treatment with organ preparations in cases in which previous thyroidized constitutional and endocrine impetus form the chief factor of the existence of the obesity.

Especially in the chief form, "the thyrogenous" obesity, one ought not lose too much time with diabetic preparations, but quickly seize upon the thyroid gland preparations without too strict dietary limitations, which, experimentally, are not very necessary here; but if there is a question of albumin, the effect of thyroid gland on the decomposition of albumin can lead to harmful results.

Success is usually obtained in oral administration of any one of the numerous preparations in the field. The purification of the active principle of the thyroid gland by Kendall (thyroxin) unfortunately has not accomplished the desired effect which one might expect of extract dosage, at a time when one is most inclined to parenteral dosage, for it has the disadvantage of requisite long treatment. Over and against the increased oxidation accomplished with thyroid gland, other organ preparations are valuable. Metabolism is only slightly increased with ovarian preparations. It is not much more increased with pituitary preparations. Of these latter, the secretion of the anterior lobe possesses a slight metabolism-increasing effect which can hardly be considered practical. In most cases the treatment with thyroid gland suffices. The numerous pluriglandular products which contain the hormones of the thyroid gland, ovary and pituitary are only effective in their thyroid gland substance. In the treatment of obesity as such — a favorable effect on many accessory symptoms must not be slighted — the preparations are superfluous if they are not accurate in their thyroid gland content, indeed they are often harmful. In no case must they be prescribed without the control of a physician.

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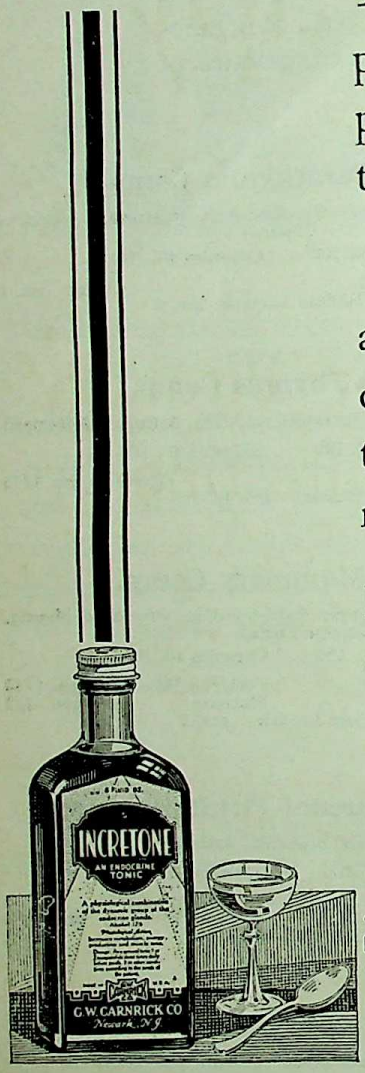
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The Action of Posterior Pituitary Preparations on the Intestine

POSTERIOR PITUITARY preparations contain a substance or substances that exert a specific action on the intestine. This action may be made use of clinically.

THE very earliest investigations of the pharmacological properties of extracts of the post pituitary lobe gave evidence of a diversity of actions — oxytocic, diuretic-antidiuretic, pressor, metabolic, etc. One of the effects of these solutions which subsequently came to be utilized in practice was the effect of stimulating contractions in the unstriped muscle of the bowel. Special preparations marked "surgical" to distinguish them from preparations for obstetrics were placed in the market for use in intestinal paralysis following abdominal operations, etc. Bell (*The Pituitary*) particularly endorsed the use of post pituitary in these conditions.

Without question this application must have been attended with a fair degree of success, yet it is interesting to note that even in the earliest reports there was evident a decided difference of opinion as to the effect of post pituitary on the intestine. The weight of evidence was in favor of an effect in stimulating contractions although reports of exactly opposite effects frequently appeared. Shamoff (1) reported:

"In view of the foregoing observations, it may be stated that there exists in the posterior lobe of the pituitary body some substance which has an action on the isolated intestinal loop resembling the action of adrenalin, a sub-

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stance moreover which may be other than that which raises blood pressure and causes diuresis. The substance is not constant in the extractives prepared in the usual ways and may indeed be inconstant in the fresh glands from which these substances are prepared. The most definite relaxations were obtained from 'Hypophysin' and from Armour's preparation made by drying the extract of the gland in vacuo at body temperature. Its presence or absence in the extracts may depend on the method of preparation and more accurate studies can only be made when this is perfected or when the active principle or principles of the gland become known and are capable of synthesis.

"As the matter stands, it may be concluded that certain posterior lobe preparations are capable of producing relaxation of the isolated intestinal loop and of inhibiting its rhythmic contractions, resembling in this respect the extracts of the adrenal medulla."

Numerous other observers reported depression of tonus and contractions and Hoskins (2) reported both depression of tonus and peristalsis in five out of six dogs injected intravenously with pituitrin. Many investigators cast doubt on the existence of a pituitary principle with a specific action in causing contractions in plain unstriped muscle. Others reported preliminary relaxation followed by subsequent increased tonus and contractions. One element of uncertainty in the several communications was a failure to take into account or report on such factors as added chemical compounds (chloretone, etc.), the pH of the solution and the existing state of tonus at the time of the experiment.

The contradictory character of these reports and reports of the same investigator of both increase and decrease of tonus and contractions made further investigation of the subject necessary. Gruber and Robinson (3) investigated the action of pituitary extracts on unanesthetized animals with a permanent Thiry-Vella fistula, noting the effect on intestinal contractions and tonus. Their work was done not only with post pituitary extracts but also with the separated elements vasopressin (the pressor principle) and oxytocin (the oxytocic principle). Their conclusions follow.

"1. Pituitary extract or pituitrin 'S' injected intravenously, intramuscularly or subcutaneously in unanesthetized dogs causes a decrease of tonus and decreased force of rhythmical contractions in the Thiry-Vella fistula of the ileum. After the temporary decrease in general tonus sudden changes in the tonus are observed which appear to be peristaltic movements. These simulate 'incomplete tetanus' of the intestine.

"2. The actions of 'Vasopressin' and of 'Oxytocin' are identically the same as that of pituitary extract.

"3. The changes in tonus of the intestine are probably not dependent upon the original state of tonus of the loop of intestine.

"4. The effects of pituitary extract, vasopressin and oxytocin are not due to the impurities choline and histamine.

"5. Histamine causes an increase in the tonus of the intestine of unanesthetized dogs.

"6. The decrease in tonus of the intestine following the intravenous injection of pituitary extract, vasopressin or oxytocin is independent of the changes in general arterial blood pressure."

Gaddum (4) reported results essentially similar, using strips of the colon, ileum and jejunum in the experiment. He also reports that particularly in the colon an inhibition usually preceded the stimulation.

"It was found that, though both preparations produced shortening of an isolated loop of the rabbit's intestine, and an increase in the peristalsis recorded by a modification of Trendelenburg's method (Garry, *Arch. exp. Path. u. Pharmakol.*, 120 : 348, 1927), vasopressin produced these effects in smaller doses than oxytocin. The effect is rather irregular and is apt to disappear after large doses, and sometimes spontaneously. The colon appeared to be more sensitive than the ileum, and the

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ileum than the jejunum. In the colon there was usually an inhibition before the stimulation. The effect on peristalsis was more regular than that on length of a segment, and was produced by smaller doses. The substance producing these effects was certainly not histamine, because quantities of histamine, hundreds of times larger than could possibly have been present, had no such effect: further, the active substance was destroyed by treatment with cold alkali. It was not the oxytocic principle, because, although the effects were produced by comparatively small doses of the international standard, a quantity of oxytocin containing twice as much of the oxytocic principle had no effect. On the other hand, this action may be due to the pressor principle. It was found that equipressor doses of the standard and of vasopressin produced similar effects on the bowel. It was not found possible to make a precise estimate of their relative potencies."

Gruber and Pipkin (5) using longitudinal excised segments of intestine, seem to have determined that the character of the effect (relaxation or contraction) induced by pituitary solutions depends upon the concentration of the preparation and the existing state of tonus. They say:

"1. High dilutions of pituitary extract if effective cause an increase in tonus and tonus oscillations in longitudinal segments of excised dog's intestine.

"2. High concentrations of pituitary extract cause an immediate loss in general tonus and complete disappearance of the rhythmic contractions.

"3. The degree of tonus normally present in the segment before the addition of pituitary extract is a factor in the results obtained. If the tonus is high, even dilute solutions may cause relaxation while if the tonus is low the strong solution may stimulate the gut.

"4. Morphine sulphate increases the tonus and, in many instances the height of rhythmic contractions, in excised segments of normal dog intestine. A similar action is noted in excised longitudinal segments taken from a Thiry-Vella loop.

(*Concluded on page 370*)

The Effect of Posterior Pituitary Preparations on the Blood Pressure

THE POSTERIOR PITUITARY BODY contains an active principle the predominant action of which is elevation of blood pressure and slowing of the heart. An unexplained depression of blood pressure preliminary to a sustained rise is usually noted.

THE rise in blood pressure, slowing of the heart and contraction of the blood vessels were among the first demonstrated effects of extracts of the pituitary body. Howell (1) showed that the principle causing this was limited to the posterior lobe. Dudley (2), Schlapp (3), and Draper (4) gave evidence that there are more than one active principle in the post pituitary and that the pressor and oxytocic principles are distinct, the diuretic-antidiuretic action apparently residing in the pressor substance. Later Kamm and his associates (5) demonstrated that a specific pressor principle can be isolated

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from the post pituitary. This is entirely distinct from the oxytocic principle but is apparently responsible for the diuretic-antidiuretic effects and in large part for the effect on smooth muscle (6). Kamm (5) found that:

"1. The posterior lobe of the pituitary gland contains two important active principles: one which raises the blood pressure and another which stimulates contraction of uterine muscle.

"2. A substantially complete separation of these two active principles has been accomplished by the employment of salting-out methods and, subsequently, by the use of appropriate solvents and precipitants.

"3. Solutions of these separated active principles have been recombined to form a pituitary extract identical with the original from which they were prepared, thus proving that no decomposition has taken place.

"4. The substantially pure pressor principle (β-hypophamine) has been obtained in the form of a white, stable, water-soluble powder 80 times as potent as the International Standard Powdered Pituitary.

"5. The separated oxytocic principle (α-hypophamine) has been obtained in the form of a white, stable, water-soluble powder which is more than 150 times as potent as the International Standard Powdered Pituitary.

"6. The pressor principle has been shown to be responsible for the diuretic-antidiuretic action of pituitary extracts.

"7. The pressor principle when tested on animals for demonstration of pressor effects shows the development of tolerance which is characteristic of active pituitary extracts. It has been shown to possess no appreciable depressor action.

"8. Both active principles are basic bodies, presumably amines."

The precise effect of pituitary upon blood pressure, however, has not been clearly established.

Most observers agree that there is a final large rise in tension, a slowing of the heart and a contraction of the blood vessels. Early observers reported that after a preliminar injection of pituitary, subsequent injectio gave either no effect or even a reversal of e fect—lowering of tension. Professor Abel, o of the earliest of all contributors to the su ject reported results of this kind. Such effec have been ascribed to a hypothetical depress substance while others have asserted that th subsequent fall in pressure is due to properti inherent in the pressor hormone itself. Kam and his associates (5) have demonstrated th the pure pressor principle is free from th inversion effect.

"We have repeated the historical experi ments of Howell (*J. Exp. Med.*, 3 : 245, 189 and of Schafer and Vincent (*J. Physiol.*, 2 87, 1899) who have shown that when doses pituitary extracts are administered intrave nously in fairly rapid succession and in rel tively large amounts a tolerance is quickl established so that after the second or thir injection no further pressor effect is demor strable.

"When plain pituitary extracts are used th typical rise in pressure may actually b replaced by a depressor action due either t the presence of traces of histamine or to th acidity. Abel (*J. Pharmacol. and Exp. Therap.*, 22 : 303, 1923) has demonstrate this depressor action even with his purifie fraction.

"In repeating this early work we have use a purified pressor fraction and find that it ac exactly like an unmanipulated pituitar extract in respect to the development of tole ance, thus showing that the product has n been modified. However, the successive lar doses fail to give any depressor action, th attesting to the degree of purification of th product."

Stehle (7) also finds that "Preparations the posterior lobe of the pituitary gland ma as described show no reversal of action upo the blood pressure upon repeated injection ten minute intervals."

Kamm does not believe the depressor acti evident in posterior pituitary extracts to

either principl oxytoc by pur "Sch demon stance the g worke by Sh *J. Ex* attach depres istan "W tracte Soxhl readil metho

Assa

(a) Co
(b) Bl
(c) Ox

"A imate being The the p large metri tamin Two depre athe hista small gland there rue "W orre ible hou

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either histamine or a special specific depressor principle, rather he believes it to be due to the oxytocic principle which he shows is extracted by pure ethyl alcohol.

"Schafer and Vincent (*loc. cit.*) not only demonstrated the presence of a depressor substance but showed that it is extractable from the glands by means of alcohol. Recent workers (for references see the excellent paper by Sharpey-Schafer and Macdonald, *Quart. J. Exp. Physiol.*, 16 : 251-280, 1926) have attached considerable significance to this depressor product, some referring to it as istamine.

"When acetone-desiccated glands are extracted with absolute ethyl alcohol in a Soxhlet extractor, this depressor product is readily removed. We have tested it by three methods, as is shown in the following table:

Assays Based on Extract from 1 G. of Desiccated Posterior Lobe

(a) Colorimetric assay for histamine	< 1 mg.
(b) Blood pressure assay for histamine	< 1 mg.
(c) Oxytocic assay	80 Oxytocic units≈ 100 mg. histamine

"According to the oxytocic assay, approximately 100 mg. of histamine is indicated as being extractable from 1 g. of gland material. The blood pressure assay, however, indicates the presence of even less than 1 per cent of this large quantity of histamine and the colorimetric test agrees in demonstrating that histamine is present only in small amounts. Two conclusions might be drawn: first, the depressor principle is not histamine but rather a substance much more potent than histamine in its oxytocic action: second, a small amount of histamine is present in the gland but in the process of alcohol extraction there is extracted simultaneously some of the true oxytocic principle.

"We believe that the second conclusion is correct. Since the oxytocic principle is soluble in alcohol, there is no reason why it should not be extracted and our results show that in six hours' extraction approximately 10 per cent of the oxytocic principle is removed."

It seems fairly certain that pure pressor principle displays little or no depressor action on subsequent injections although numerous observers describe a drop in pressure preliminary to a sustained rise. Gruber and Kountz (8) report results of this kind. They attribute to the preliminary fall in blood pressure a very important function in causing the subsequent sustained rise in pressure. They state:

"In the unanesthetized dog following the injection of pitressin the heart rate at first decreases during the primary rise in blood pressure, then it accelerates during the drop in blood pressure and decreases again during the secondary prolonged rise in blood pressure. Similar findings were recorded in dogs under either chloretone or ether anesthesia.....

"The acceleration in heart rate which occurs during the fall in blood pressure after the injection of pitressin is mainly if not wholly a reflex compensatory phenomenon. The sudden fall in blood pressure reflexly exciting the cardio accelerator center, is an attempt on the part of the cardio-vascular system to maintain a normal blood pressure.

"The slowed heart rate caused by the injection of pitressin is partly a reflex due to stimulation of the cardio-inhibitory center through the depressor nerve, and partly due to a direct action upon the heart muscle itself, the latter due probably to injury through vasoconstriction of the coronaries."

Stehle (*loc. cit.*) also notes a depression of pressure on first injection. "Tracing 2, which is not representative of the results as a whole, shows two blood pressure maxima on first injection and the fall between the rises is to a point below the pressure just prior to the injection. This is not to be regarded as a reversal of action since it occurs with the *first* injection and does not appear with later injections. What caused this effect is not clear but we hope to make the phenomenon the subject of further study."

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The initial depressor action of pituitary extracts is not yet fully explained. The existence of a specific depressor principle is not definitely excluded. The cardio-vascular compensatory mechanism may explain it without recourse to such a substance. A reversal effect on repeated injections seems to be disproved if pure pressor preparations are used. Apparently when the initial rise of pressure occurs the heart action slows; when the drop in pressure comes, the heart action increases and then during the prolonged characteristic rise of pressure the heart again slows up.

1. Howell, W. H., *J. Exp. Med.*, 3 : 245, 1898.
2. Dudley, H. W., *J. Pharmacol. and Exp. Thera* 14 : 285, 1920.
3. Schlapp, *Quart. J. Exp. Physiol.*, 15 : 327, 1925.
4. Draper, W. B., *Am. J. Physiol.*, 80 : 90, 1927.
5. Kamm, O., Aldrich, T. B., Grote, I. W., Rowe, W., and Bugbee, E. P., *J. Am. Chem. Soc.*, 50 : 5 Feb., 1928.
6. Hjort, A. M., *Endocrinology*, 12 : 496, 1928.
7. Stehle, R. L., *Am. J. Physiol.*, 88 : 724, 1929.
8. Gruber, C. M., and Kountz, W. B., *J. Pharma and Exp. Therap.*, 39 : 275, July, 1930.

Clinical Observations concerning Respirator Basal Metabolism

(Translated from the article by Prof. F. de Quervain and Dr. F. Pedotti, First Assistant Physician at the Surgical Clinic, Berne.)

(*Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 39 : 646, 1926.)

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(Continued from Vol. XIV, No. 5)

II. General Relationship between Basal Metabolism, Pulse, Volume per Minute and Respiratory Quotient

In accordance with the survey of our experimental material we have concerned ourselves with the question of whether the elements concerned: Pulse, volume per minute and respiratory quotient, have a constant relation and whether this relation could accomplish anything for the determination of the basal metabolism for clinical purposes, and eventually for the thyroid gland. For the investigation of this problem we have made distribution tables of the individual relationships a we shall discuss the problem in the light these tables. We have worked out the tabl for the collective material as well as for t thyroid gland material alone, but we give t latter here again since only they are autho itative for the solution to the problem pr sented.

(a) *Relationship between Respiratory Quotie and Basal Metabolism*

We know from the respiratory quotie $\frac{\text{Vol. } CO_2}{\text{Vol. } O_2}$, that the higher it is the more ca bohydrate is burned and the lower, the mo fat is consumed. In cases of pure fat co

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sumption it is 0.71, in pure carbohydrate consumption 1.0. If an individual who has fasted for 12 hours after a light meal shows a high basal metabolism, he can not proceed further at the cost of administered carbohydrate, but he must first of all resort to the body itself. Hence the respiratory quotient drops, and the lower it goes, the higher the basal metabolism and the more the body fat must be assailed. It is of interest to investigate how far this theoretical supposition is carried out in practice. In the accompanying distribution table

Table 4. Respiratory Quotient and Basal Metabolism

0

R.Q.	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-x Basal Metabolism %
To 0.72			• • • • •	• • • • •	• • • •		• • • • •		•		•	•	•	•
0.73-0.75			• • •	• • • • • •	• • • •	• • • •	• • •	• •	• •	•			•	
0.76-0.78	•	•	• • • •	• • • •	• • • • • •	• •	• • • •	•	• • •	•		•		
0.79-0.81	•		• • •	• • • • •	• • • • •	• •		•		•				
0.82-0.84		• •	• • • •	• • • • • • •	• • • • •			•						
0.85-0.87		•	• •	• •	•	•			•					
0.88-0.90		•	•	• • • •	• • • •									
0.91-0.93				• •	• •					•				
0.94-0.96					•									

0

the majority of values group themselves pretty well about the null line of basal metabolism and about the average value of respiratory quotient usually considered to be about 0.82. If the distribution of values be considered, there is a very evident interdependence, in that the further toward the plus calculation the basal metabolism goes the lower the respiratory quotient is. It is evident that in a larger amount of material this will be still more impressive. On the other hand we observed minus quantities of basal metabolism in the lowest respiratory quotients. The state of interdependence is only relative and we can not with any sort of certainty, draw conclusions from the amount of the respiratory quotient. The fact that very variable height of respiratory quotient is to be found even in basal metabolism values grouped about the null line is associated with the fact that in individual experiments, even with the same basal metabolism fat consumption extends to various levels, and that the body, despite the abundance of its last carbohydrate alimentation, and its level of glycogen content rapidly attacks its own fat in various manner.

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(b) *Relationship between Pulse Frequency and Basal Metabolism*

That a relationship must exist between pulse frequency and basal metabolism is shown in the comparison between the Basedow patients and the cretins. By a glance at the distribution table, No. 5, without further indication, one can see that the values run diagonally from the lowest pulse frequency and the lowest basal metabolism to the highest frequency and the highest basal metabolism. Likewise, it can be seen that the greatest number of findings are compactly grouped about

Table 5. Pulse Frequency and Basal Metabolism

Pulse-	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-x Basal Metabolism %
40-49			·											
50-59		· ·	· · ·	· · ·	·									
60-69	·	·	· · · · · ·	· · · · · · · ·	· · · · ·									
70-79		· ·	· · · · · · · · ·	· · · · · · · · · ·	· · · · · · · · · ·	· ·								
80-89			·	· · · · · · ·	· · · · · · · · · ·	· · · ·	· · ·							
90-99	·			· ·	· · · · ·	·	·	·						
100-109			·	· ·	· · ·	· ·	· · ·	· · ·	·					
110-119				·	·		·	·	·		·	·		
120-129					·		· · ·		· · · ·	· ·		·	·	·
130-139							·			·			·	

the pulse rates from 60 to 89 and about the basal metabolism value of ± 10 per cent. This relationship only holds good, however, for our material. A series of heart disease cases would give an entirely different picture, for in this case an increase in pulse frequency is not synonymous with the rise of the combustion process. Certain deviations are also found in thyroid gland cases, for here, too, factors unassociated with the thyroid gland are not rarely involved. The pulse frequency, then, permits us to draw a fairly good, but not absolute conclusion concerning the basal metabolism.

The relationship between pulse frequency and basal metabolism was the subject of another investigation. According to Means and Minot an increase of B. M. of around 50 per cent corresponds to an average rise of pulse frequency of about 65 per cent. The same numerical ratio was found by these authors for leukemia, in which instance, as is well known, a specific rise of B. M. was found. Our distribution tables approximately agreed with the findings of Means and Minot. The report of these authors is noteworthy, namely that in healthy people an increase of about 50

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per cent in metabolism during muscular work, implies an increase of only 25 per cent in pulse frequency.

Field and Back have very recently compared the volume of heart beat in M. Basedowii and in myxedema and found in the former an increase of about 16 per cent and in the latter a decrease of about 50 per cent.

(c) *Relationship between Volume per Minute and Basal Metabolism*

Without further explanation it is evident that the volume per minute is closely related to the basal metabolism, *i. e.*, in general a high value of volume per minute signifies a high rate of basal metabolism and *vice versa.* In the distribution table this fact is very prominent. Here, also, the majority of findings are grouped about the normal figures for basal metabolism of ±10 per cent and the normal volume per minute of 5.0 to 6.7. The relationship between this and basal metabolism is stricter than that between pulse frequency and basal metabolism but here, too, there occur several sharply variant, disperse values, which indicate that the determination of volume per minute can not be given preference over determination of basal metabolism. We

Table 6. Volume per Minute and Basal Metabolism

	0													
	−	−	−	−	+	+	+	+	+	+	+	+	+	+
Vol. per min.	30-39	20-29	10-19	0-9	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90-x Basal Metabolism %
3.5-3.9		..	.											
4.0-4.4	.		....	...	...									
4.5-4.9			...	.	...									
5.0-5.4			....	....	....									
5.5-5.9		.	...	....	.... .	..	.							
6.0-6.4				.... .	....	.	....	.			.			
6.5-6.9				...	...	...	....		.					
7.0-7.4		.		.	..		.	.	....	.				
7.5-7.9		.			.	.	.	.		.				
8.0-8.4						.		.	.					
8.5-8.9							.	.						
9.0-9.4	.					.		.				..		
9.5-9.9										.				.
10.0-10.4														
10.5-10.9													..	
	0													

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sought to hold the volume per minute at an approximately constant value by standardization, therefore we commenced with volume per minute per square meter body surface, and thus determined the normal volume per minute per meter for various ages and for both sexes.

$$\text{Meter volume per minute, MMV} = \frac{\text{Volume per minute in liters}}{\text{Body surface in m}^2}$$

We have converted Table 6 in this manner and the volume per minute of each case has been brought into relation with the basal metabolism of the case. This table (Table 7) gives a picture similar to that in Table 6.

This shows also a rather high degree of distribution, so that the meter volume per minute as well as the volume per minute gives an approximate indication of the basal metabolism, but nothing more than this. It is very evident that the distribution arises from the varied composition of the expired air.

Table 7. Meter-Volume per Minute and Basal Metabolism

M.-Vol. per min.	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-x Basal Metabolism %
2.5-2.9	.	.	. . . .	. . .	. .									
3.0-3.4		.	. . . .	. . . .	. . .		.							
3.5-3.9			. . . .	. . . .	. . . .	. .	. . .							
4.0-4.4		.	.	. . . .	. . . .	. . . .	. . . .	.	.	.	.			
4.5-4.9				. . . .	. .		.	.	. . .					
5.0-5.4		.		. .		.	. .	. .	. .	.				
5.5-5.9					. . .	. .		.		.		. .		
6.0-6.4	.	.												
6.5-6.9							.						.	
7.0-7.4													.	.

0 0

We have converted Table 6 in this manner and the volume per minute of each case has been brought into relation with the basal metabolism of the case. This table (Table 7) gives a picture similar to that in Table 6.

This shows also a rather high degree of distribution, so that the meter volume per minute as well as the volume per minute gives an approximate indication of the basal metabolism, but nothing more than this. It is very evident that the distribution arises from the varied composition of the expired air.

(*d*) *Relationship between Pulse Frequency and Volume per Minute*

This is in agreement with the general idea that pulse frequency and volume per minute run parallel with one another to a certain extent. This is indicated in the survey table, No. 8. There are some discordant values here also, which originate partly from the inability of certain patients to adjust themselves to unrestrained breathing with the apparatus. Repeated attempts with the same patient brought about a decrease of these extreme values.

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Table 8. Pulse Frequency and Volume per Minute

Pulse	3.5-3.9	4.0-4.4	4.5-4.9	5.0-5.4	5.5-5.9	6.0-6.4	6.5-6.9	7.0-7.4	7.5-7.9	8.0-8.4	8.5-8.9	9.0-9.4	9.5-9.9	10.0-10.4	10.5-10.9 Liter vol. per minute
40-49			•												
50-59	•		•	• •	•	•		•	•						
60-69	•	• •	• •	• • • • • • • • • •	• • •	• • • •	• •								
70-79	•	• • • •	• •	• • • • • • • • • • • •	• • • • • • • • •	• • • • • • •	• • • •	•				•			
80-89		• •	• •	• • • •	• • • • • •	• • •	• •	• •	•	•					
90-99		•	•	• •	• •	• •	•			•		•			
100-109				• •	• • •	• •	• • •	• •	• •			•			
110-119						• • •		•		•		•			
120-129					•	•	• •	• • • •			•	•	• •		•
130-139									• •						

Table 9. Respiratory Quotient and Pulse Frequency

R.Q.	40-49	50-59	60-69	70-79	80-89	90-99	100-109	110-119	120-129	130-139 Pulse
To 0.72		•	•	• • • • • •	• •		• • • •	• • • •	• • • •	• •
0.73-0.75		•	• •	• • • • • •	• • • • • •	• • •	• • •	•	• • • • •	
0.76-0.78		•	• • • •	• • • • •	• • • • • • • • •	• • •	• • • •	•	• •	•
0.79-0.81	•	•	• •	• • • • •	• • •	• • • •	•		• •	
0.82-0.84		• •	• • • • • •	• • • • • • • •	• • •		• •			
0.85-0.87		• •	• • •	• •			•			
0.88-0.90			• • • • •	• • •	•					
0.91-0.93					• •	•				
0.94-0.96			•	•						

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(*e*) *Relationship between Respiratory Quotient and Pulse Frequency*

What has been said up to the present would imply that, in the matter of thyroid gland pathology, there was a certain association between respiratory quotient and pulse frequency, namely the lowest quotient is to be expected with the highest pulse frequency. The accompanying distribution table, No. 9, brings this out in fact, certainly it has a broad tendency to the lower values. According to the above stated facts, the association would be more disrupted if the majority of disease of the organs of circulation were investigated

(*f*) *Relationship between Respiratory Quotien and Volume per Minute*

In this instance thyroid gland patient possess a certain relationship, in as much a the highest volumes per minute are found wit the lowest values for respiratory quotient an *vice versa*. Table 10 demonstrates this, bu exhibits a strong tendency to lower values fo both factors.

Table 10. Volume per Minute and Respiratory Quotient

R.Q.	3.5-3.9	4.0-4.4	4.5-4.9	5.0-5.4	5.5-5.9	6.0-6.4	6.5-6.9	7.0-7.4	7.5-7.9	8.0-8.4	8.5-8.9	9 0-9.4	9.5-9.9	10.0-10.4	10.5-10.9 Liter vol. pe minute
To 0.72		. .	.	. . . . .	.	. . . . .		. .	.		.	.	.		.
0.73-0.75		. .	.	. . . .	. . . . .	. .	. . . .	. .		.		. .	.		.
0.76-0.78			. .	. . . .	. . . . . .	. . . . .	. . .	. .	. .	.		. .			
0.79-0.81		.	. . .	.	. . . .	. . . . .	. .	. .	.	.					
0.82-0.84	. .	. . .	.	. . .	. . . . .		. .	. . .							
0.85-0.87		.	.	. . .	.		.		.						
0.88-0.90	.	.		. .	.	. . . .	.		.						
0.91-0.93		. .			.										
0.94-0.96							.								

If we ask ourselves now, simply, which of the values derived can be applied for the purpose, at least, of approximate valuation of gas metabolism determination, according to what has been said thus far, pulse frequency, volume per minute and meter-volume per minute are to be taken into account. Pulse frequency exhibits the most accurate parallelism, if we exclude the bulk of thyroid gland material. It ceases to be of value, however, as soon as there arises a question of differential diagnosis between hyperthyroid condition and, for example, a pure cardiac acceleration of pulse. The joint consideration of the volume of breath in thyroid gland cases was determined according to reliable calculation, but it was quite impossible for us to obtain a mathematical formula which, with total constancy of pulse frequency and volume per minute of breath, would give parallelling value for basal

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metabolism. Whether the joint consideration of volume of heart beat (Means, Field and Bock) will yield us any further information, must be obtained by the investigation of a greater number of hyper- and hypothyroid cases. For the present we can say that the determination of basal metabolism can not be obtained by any simple calculation by arithmetical method.

III. Relationship between Basal Metabolism, Body Weight and Body Length

We commenced with the question of whether, in cretins with and without goiter, the body length, namely the degree of dwarf growth, bears any relation to the height of the basal metabolism. The accompanying distribution table, No. 11, shows that such a relation is not evident. Because of the difficulty of performing the gas metabolism experiment on cretins in general, and because of the impracticability of most cretins of Degree III, we do not wish to put much stress on this presentation. At any rate the following fact impressed itself on us:

Table 11. Body Length and Basal Metabolism (only Cretins)

	0					
	−	−	−	−	+	+
Body length	30-39	20-29	10-19	0-9	0-9	10-19 Basal Metabolism %
115-119				.		
120-124						
125-129		.	.	. .		
130-134			.	.	. .	
135-139		. . .	.	. . .	.	
140-144				.	.	
145-149			. .	.	.	
150-154	.		. . . .	. .		
155-159				. . . .	.	
160-164	.	.	.	.	.	
	0					

Cretins with atrophic glands must reckon with a certain lack of gland function in their body. The thyroid gland function which still remains in them is only sufficient for the needs of a dwarf body, rather than for a normal person of their age, for whom the standard tables were constructed. A part of the anticipated deficiency of basal metabolism in a normally constructed adult with acquired myxedema, for example, is here compensated by the arrested dwarf growth. Therefore, the dwarf cretin can possess a "well behaved" basal metabolism if he remains small. Hence arise the compensation processes mentioned elsewhere, which are developed more easily in cretins with thyroid gland insufficiency from youth, than in cases of acute, acquired thyroid insufficiency.

Now we investigated further, whether an association could be demonstrated between basal metabolism, weight and body length, *universally* in thyroid gland material. Indeed the Du Bois formula of body surface is concerned with body weight and body length. This formula, however, refers to *normal* bodies. If we are able to demonstrate a relationship in the distribution table, assuming the correctness of the formula, this must arise from a *pathological* factor. If we consult the body weight from 39 kg. on, which comprises mostly youthful individuals in whom entirely different circumstances are involved, it appears (Table 12) that at the lowest body weights the distribution tends toward the highest basal metabolism and with increasing body weight it is more and more confined to the lower basal metabolic values. The highest basal metabolism and the most intense combustion hence will be found in the thinnest persons. Since this table is concerned only with the thyroid gland, we must recapitulate this evidence and say that a higher basal metabolism with a more rapid combustion of body fat leads to decrease in weight and conversely — a result, then, which was to be expected. In order to

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Table 12. Body Weight and Basal Metabolism

Body Weight	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-x Basal Metabolism %
20-24				·	·									
25-29			·	·	·									
30-34		·	·	·	· ·		·							
35-39		· ·	·	· · ·										
40-44			· ·	· · · ·	· · · · · ·	· ·			· · ·					·
45-49	·	·	· ·	· · · · · · ·	· · ·	·	· ·	·	·	·	·		·	
50-54	·		· · · · · ·	· · · ·	· · · · · · ·	· ·	· · · ·	· ·	·	·			·	
55-59			· · · ·	· · · ·	· · · · · · ·		·	·		·		·		
60-64			· · · ·	· · ·	· · · · · · ·	·	·		·					
65-69			·	· · ·		·	·	·				·		
70-74		·	·	· · · ·	·	·	· ·							
75-79				·										
80-84														
85-89				·		·								

estimate the validity of the Du Bois formula, the same kind of calculation must be undertaken for *healthy* thyroid individuals.

Also, the comparison of body length and basal metabolism (Table 13) gives evidence of a certain regularity anticipated from the synthesis of the material. With increasing body length the distribution inclines toward the side of high basal metabolism. For the reliability of the Du Bois formula, the same applies here as above.

IV. Relationship between Basal Metabolism and Rat Test

The rat test according to Asher-Streuli, was undertaken on 40 cases of the material under discussion. Part of these cases are contained in the work of Messrs. Pedotti and Branovacky. The present presentation is an expansion of the latter. The principles on which the comparison is made are analyzed in the above mentioned work; so that we do not need to report them here. We qualify the results as satisfactorily agreeing (even if not always quantitatively parallel), if both the rat test and the gas metabolism are definitely on the plus side, if both hover close to the null line and if, in the case of negative gas metabolism value, the rat injected with arm blood serum reacts with null. (The latter is legitimate since in most cases of minus gas metabolism results, the venous blood from the arm does not influence the rats experimentally.)

We consider the agreement inadequate, for

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Table 13. Body Length and Basal Metabolism (all cases excepting the Group Varia)

Body length	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-x Basal Metabolism %
110-119.9				·										
120-129.9		·	·	· · ·	·									
130-139.9		· · ·	· · ·	· · · ·	· · · ·									
140-149.9		·	· ·	· ·	· · ·									
150-159.9	·		· · · · · · · ·	· · · · · · · · · ·	· · · · · · · · ·	· · · · ·	· · · · ·	· · ·		·	·			·
160-169.9	·	·	· · · · · · · ·	· · · · · · · ·	· · · · · · · · · ·	· · · · ·	· · · · ·	· ·	· · · · · ·	·		· ·	· ·	
170-179.9			·	· · · ·	· · ·		·							
180-189.9							·			·				

example, if the rat with a gas metabolism of +20 per cent reacts only weakly positive. We qualify the results as diverging if in the instance of pronounced positive gas metabolism result, the rat does not react positively, or reacts with an abnormally low gas metabolism (under −10 per cent).

Measured according to this criterium, our cases from 40 investigations show

30 times satisfactory agreement = 75 per cent
4 times inadequate agreement = 10 per cent
6 times divergence = 15 per cent

The results agree with those reported by Pedotti and Branovacky and show that the agreement is as broad as may be expected, considering the complex biological methods and the source of error in the nature of the thing itself. An example will serve to illustrate the parallelism of both methods of investigation:

Control No. 106, female patient, 25 years, medium degree of Basedow for 2 years	Basal metabolism	Experiments on rats
9/5/23 (before operation)	+21 %	+++
23/5/23 (12 days after operation, influence of wound resorption)	+14 %	0 to+
13/8/23 (3 mos. after operation)	− 6.5%	0

All three results agree, then, on condition that the one negative result of the rat experiment arose from a profound minus value of basal metabolism.

The relationship between gas metabolism, rat test and tadpole test and the calculation of the rat experiment with arm blood, according to the latest experiments, will be reported by Dr .Branovacky himself in a special article.

(To be concluded)

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Practical Therapeutics

Endocrine Treatment of Retarded or Abnormal Mental Development

DRUG therapy of psychic abnormalities has been notoriously ineffective. The mental diseases are in many instances practically beyond the possibility of any treatment since they arise from a constitutional, hereditary basis. The inherent tendency to react to the environment can not be changed and the evolution of a mature abnormal mind follows a natural course of development, just as certain as the normal type in normal individuals. The course of the classical insanities is therefore marked by an unchangeable progression of well marked, well recognized phases.

The "personality" of the individual is itself a fixed, unchangeable factor so far as the efforts of the physician are concerned. Minor degrees of mental abnormality, erratic behavior not classed as mental disease and border line cases present this constitutional factor as well. Many individuals display peculiar behavior only under stress of adaptation to environment and would otherwise fail to exhibit any abnormality. The physician must always study mental disease from the standpoint of a mental mechanism reacting to the environment.

These constitutional "tendencies" resulting from congenital "psychopathic inferiority" may give diverse symptoms which may make classification of essentially the same types rather difficult. The apparent differences lie either in the different environmental changes to be met or to the different responses to meet them. Underlying is the same abnormal, perverse, instinctive tendency to react to situations in a different manner from "normal" individuals.

Certain types of mental abnormality and conditions of failure of normal development of the mental mechanism have been definitely related to demonstrable defects of endocrine glands. Whether these gland defects are coordinate with other physical retrograde changes or subordinate to more profound changes of constitutional nature can not always be determined. The rather constant association, however, of certain mental defects with specific endocrine dysfunction has been frequently noted.

Moreover, the effect of the internal secretions on tissues and on mind is so great, that even if the ultimate cause lies beyond the endocrine system the actual clinical picture is largely the immediate effect of the abnormal endocrine make-up. No one can doubt the enormous influence on mind and body of the thyroid, pituitary, sex glands or adrenal cortex. Usually more than one gland is involved. The use of such endocrine substances as anterior pituitary, adrenal cortex, thyroid and pineal has a large field of application particularly in those early cases in which deviation from normal is diagnosed and the associated endocrine defect recognized. Delayed mental development with normal characteristics is also a promising field.

Endocrine Dystrophies and Mental Subnormalities. — William G. Downs, Jr. (*Ann. Int. Med.*, 2 : 810, Feb., 1929.)

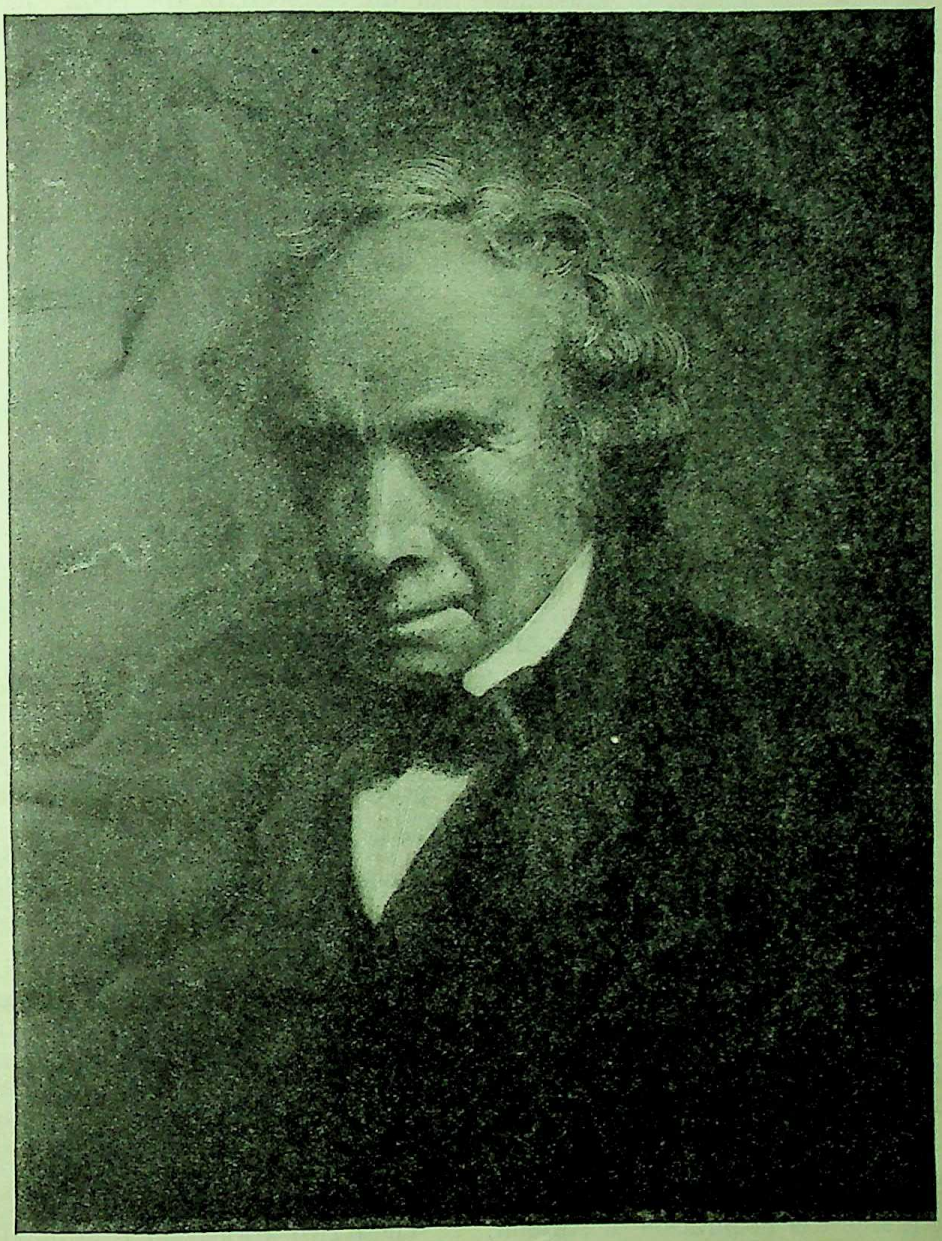
While marked endocrine types are relatively infrequent among the population at large, a very great per cent of the patients in any institution for the care of mental defectives displays unmistakably the symptoms of endocrine defects. As Downs says, it is only to be expected that if the glands of internal secretion have any effect whatever upon the organ-

(*Continued on page 371*)

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The Doctor's Page



WILLIAM STOKES
(1804-1878)

When first meeting William Stokes, Thomas Carlyle described him as a "rather fierce, sinister looking man, . . ." who, as the evening wore on "became more and more gloomy, emphatic, and contradictory." A glance at the accompanying likeness of him, made at about the period when Carlyle met him, seems to confirm such a characterization; but a

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study of the life and work of this great Irish physician discloses a vast difference between his personality and character and his appearance.

William Stokes, son of Whitley Stokes, himself a distinguished Irishman, of illustrious lineage comprising famous engineers, lawyers and public servants since the Norman Conquest, was born in Dublin, July, 1804. His boyhood was spent at his father's country house, Ballinteer, in Dublin hills. William exhibited no special ability as a youth; he was mentally and physically indolent, and the fact that his father was a staunch believer in home instruction encouraged this lackadaisical attitude. He was no athlete: instead of indulging in boy's sports he preferred to hide away in a beech hedge he called his "nest", to while away hour after hour romanticizing over Sir Walter Scott's recently published "Scottish Border Ballads." An incident once occurred, it is reported, which disclosed to him his mother's grief at finding him so disinterested in profound subjects, and virtually overnight he changed into a studious diligent pupil. He admitted later that he had missed much by not receiving systematic college training and he was subsequently a firm advocate of such education. However, there were some benefits to be derived from the education he received at home, for he had the privilege of close association with the reputed scholar and mathematician, John Walker, who was his tutor in Latin, Greek and Mathematics. He also met the distinguished friends of his father's coterie, such as Henry Grattan, Irish lawyer, statesman and orator; James Martineau, English minister and writer; O'Conor, the landscape painter; J. Parsons, eminent lawyer; and Petrie, archeologist, musician and painter, who remained one of his close friends throughout life and whose life he edited and published ("Life and Labours in Art and Archeology of George Petrie").

The first inclination toward a scientific career was evidenced when Stokes made the acquaintance of James Apjohn. From that time forth, under the inspiration of Apjohn, he sought studies in Clinical Medicine at Meath Hospital, in Chemistry in the laboratory at Trinity College and at the Royal Society of Surgeons. For two years he worked in the chemical laboratory of Professor Thompson, and subsequently, on advice from his father, proceeded to Edinburgh for the medical degree. Here he met Professor Alison and chanced to be of some service to him. S great was his admiration for this man that h voluntarily accompanied him night and da as Alison made his rounds. From him Stoke probably derived his sympathy and regar for the suffering of the poor. Eventually i his own practice and clinical work he pr longed the charitable work which Alison ha done in the way characteristic of Aliso Nothing was too much for a needy patient wh came under his observation, no heart wa heavy but that he made an attempt to lighte its burden.

At the period when Stokes was a medica student the French school of auscultation an percussion was in the ascendency. Laenne was having a decided influence on medicine in the United Kingdom. Stokes saw pos sibilities in the methods and even before h was a fully qualified physician he publishe (1825) in Edinburgh, a small treatise entitle "Introduction to the Use of the Stethoscope," which netted him £70. This was followed b further contributions on the stethoscope an also to the treatment of diseases of the thorax which apparently were the foundation for hi great treatise on diseases of the chest eleve years later. Several papers on the steth oscope had already been published (especiall Laennec's "Mediate Auscultation," 1819) but this work of Stokes was deemed the "firs systematic treatise." He was ridiculed by hi teacher for devoting himself to the mastery o the instrument, but the success and fame o his later work on the chest attested th sagacity of his study. In the autumn of 182 Stokes received the degree in medicine a Edinburgh and thereafter was appointe Physician to the Dublin General Dispensary a post virtually without pecuniary reward but which he filled to the satisfaction of eve the most meticulous. In 1826 an appoint ment took him to Meath Hospital where h was associated with Robert James Graves destined to be one of his closest friends an most esteemed companion and associate Stokes later edited Graves works.

These two worked hand in hand untiringl during the typhus epidemic in Dublin in 1826 as well as in the Asiatic cholera siege whic swept Ireland in 1832. Stokes also lecture at Meath Hospital and published man papers in the *London Medical and Surgica Journal*. During 1833 and 1834 the *Londo Cyclopoedia of Practical Medicine* receive from him contributions to Volumes II and III

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and in 1834 Stokes took up the Editorship of the *Dublin Journal of Medical Science*, to which he brought papers on thoracic pathology in particular. A paper entitled "Peritonitis from Perforation of the Serous Membrane," which introduced the use of opium, and revolutionized the treatment of this disease, appeared between 1833 and 1835. The work on "Diseases of the Chest" actually began in 1835, but on account of ill health, it was intercepted for a trip to the Continent, to Holland, Belgium and up the Rhine. He returned much improved and greatly inspired, with the result that in 1837 this work was offered to an already enthusiastic public and was "hailed with delight" by all classes of scientific workers. Actually in this publication Stokes augmented and corrected the material which Laennec and Corvisart had already presented. The latter two had given, primarily, phenomena of thoracic diseases, so that the minutely descriptive and diagnostic work of Stokes was practically a new and certainly an original treatment of the subject. No one was better qualified than he to systematize the subject matter and to introduce it in excellent language to the English speaking profession. The intelligible graphic terms in which he couched his ideas is still a source of admiration. As a diagnostician he ranks high, for he emphasizes that "physical signs only reveal mechanical conditions which may proceed from the most different causes, and that the latter are to be determined by a process of reasoning on their connection and succession, on their relation to time, *and their association with symptoms*." This book is divided into nine sections; the second, dealing with bronchitis, is reported to be the most exhaustive and voluminous. The detailed descriptions, "a series of living pictures of disease," are invaluable. Englishmen welcomed the work warmly; in Germany it was declared "unequalled since Laennec."

Honorary degrees came in from all sides. He was made Doctor of Medicine in the University of Dublin, Fellow of King and Queen's College of Physicians in Ireland, Honorary member of the Imperial Academy of Medicine in Vienna, of the Royal Medical Societies of Berlin, Leipsic, Edinburgh, Ghent, the Grand Duchy of Baden, of the Medico-Chirurgical Society of Hamburg and of the National Institute of Philadelphia. His works were translated into French and German and revisions were made for American publication. In 1837 the first American edition of "Lectures on the Theory and Practice of Physic" was published in Philadelphia.

To William Stokes credit is due for the founding of a new Society in the United Kingdom: the Pathological Society of Dublin (1838) "not devoted to any school or system, but eclectic, neither regarding morbid anatomy as its first object, but as subsidiary to pathology considered in its widest sense, and embracing the history, symptoms, diagnosis, and treatment of each case of disease submitted to the Society." To the fulfillment of these aims Stokes gave many years of his life and was responsible for unnumbered contributions.

A treatise on "Medical Education," published in Dublin in 1861, is a splendid example of the literary ability with which Stokes pursued each subject he chose. In the same year the honorary degree of LL. D. was conferred upon him by Edinburgh. The University of Oxford in 1865 presented him with the honorary award of D. C. L. and in 1874 the Royal Irish Academy inaugurated a new institution by electing Stokes, a physician and the first to be chosen for this post, president. Ill health, however, permitted him to serve for two years only, after which he resigned. One other rank of distinction must be mentioned, namely that of Regius Professor of Medicine at the University of Dublin, which came to Stokes after the death of his father (1845).

Besides a successful teacher and writer Stokes was a matchless story-teller, a born conversationalist. His writings, whether scientific or literary, were expressed in excellent English; his letters to his family and friends, while he travelled over the Continent, are virtually literary gems in their beautiful descriptions of the things he saw and the people he met. His Celtic wit is refreshing and characteristic. Shakespeare and Scott were his chosen writers. He was well versed, not only in the works of these men but also in the poetry and folklore of his own and other countries.

The home life of the Stokes household must have been ideal, with such a fascinating host to preside. The family circle was very close, for Stokes was exceptionally fond and thoughtful of his wife and children; he gave them unusual opportunities to meet and enjoy illustrious and interesting persons who visited the house for evenings of diversion. There

(*Concluded on page 374*)

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Medical Subjects by Famous Masters



"A DOCTOR FEELING A PATIENT'S PULSE," by Jan Havicksz. Steen (1626-1679)
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Editorial Comment

The Journal of Organotherapy

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Suprarenal Cortex and the Secondary Sex Characteristics

SOME relationship of the suprarenal cortex to the secondary sex characteristics, both to their development and to their subsequent maintenance has long been recognized. Deficient sex development is found to be frequently associated with small cortex; sexual precocity with cortical hypertrophy; changes in the cortex occur during estrus; feeding the gland increases the rate of growth of the testes; and most spectacular of all, the curious change from the secondary sex characteristics of the female to those of the male (virilism) are constantly found to be associated with neoplastic growths of the cortex. Riddle found the weight of the cortex constantly increased at each ovulation cycle, an increase averaging 40 per cent. L. C. Wyman found that suprarenal insufficiency in rats results in partial or complete inhibition of estrus, the extent of the insufficiency being directly related to the degree of disturbance of the ovarian function. R. C. Moehlig gave experimental evidence to show that the cortex is fundamentally related to the development of all mesothelial tissue and that both development and subsequent normal function of the sexual glands are dependent upon the normal functioning of the suprarenal cortex. Hartmann and his associates have demonstrated that these effects are due to a hormone by extracting a potent substance which they call "cortin." With this substance animals in which the cortex has been removed may be kept alive and by the use of subminimal amounts the symptoms of suprarenal insufficiency may be maintained.

Abstracts of articles by F. Ricci and by L. Langeron, E. Decherf and Danes appear below. They are typical of many which have been previously reported and are rather striking cases of this curious influence of the adrenal cortex on sex.

Suprarenal Virilism. — F. Ricci. (*Il Policlinico*, Oct. 1, 1928.)

After a review of the cases of this affection already reported, F. Ricci reports the case of a woman of 34 years who presented simultaneous crises of pain in the right hypochondrium with lumbar irradiations, a disappearance of menstruation and appearance of abundant hair on the chin and upper lip, then on the abdomen and legs; at the same time the voice became heavier. There was noted edema of the lower members, a collateral lumbar circulation and of the subumbilical, and palpation revealed the presence in the right hypochondrium of an elastic tumor, of unequal consistency, distinct from the liver, and heavy. The spleen was hypertrophied and hard. The liver slightly enlarged; the urine slightly albuminous; examination of the blood showed nothing abnormal outside of the presence of some myelocytes and neutrophil metamyelocytes. Catheterism of the right ureter was possible only to a length of 20 cm. and pyeloureterography showed a sudden elbow in the region of the third lumbar. Operation disclosed a tumor as large as the head of a fetus,

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enclosing the kidney, which was, however, distinct from it. Upon section it presented degenerated zones and zones having the appearance of fish meat. The patient died the evening after the operation.

Histological examination showed that this tumor had all the characteristics of a suprarenal tumor; it presented polymorphous elements, with large elements in the midst of ordinary cells, with hyperchromatic nucleus and with protoplasm of cylindrical form. There were also giant multinucleated cells and necrotic cells interposed between the well preserved cells; the stroma was represented exclusively by blood capillaries as is the rule in suprarenal tumors. Finally the cells with nuclear fragmentation and karyokinesis confirmed the malignant character of the tumor.

The author shows the interest of this case which confirms the existence of relations between the suprarenal and the development of secondary sexual characteristics.

Suprarenal Cortex Epithelioma with Virilism and Hirsutism. Localization by Pneumoperitoneum. Surgical Extirpation. — L. Langeron, E. Decherf and Danes. (*Bull. et mém. Soc. méd. hôp. Paris*, **45** : 436, Apr. 1, 1929.)

The rarity of suprarenal tumors induced the authors to report the following case: virilism, amenorrhea, hirsutism, hypertension, glycosuria, and emaciation in a young girl of 20 years; localization by pneumoperitoneum of a tumor in the left suprarenal region; surgical extirpation, sudden death 36 hours after the intervention; histologically: suprarenal cortex epithelioma.

Abstracts

Contributions to Ovarian Transplantation after Loss of Both Sex Glands. — Siegert. (*Med. Klin.*, **25** : 1808, 1929.)

For the most part autoplastic ovarian transplantation has not brought about the expected result. Symptoms of insufficiency of various sorts could not be ameliorated, nor could menstruation be induced. The test with injections of substance from the anterior lobe of the pituitary to stimulate the function of the sex glands was unsuccessful. According to clinical experience with the cases observed it must be assumed that the implanted tissue is more or less decomposed and that it is hence impossible to substitute for the loss of the ovaries in sexually mature women.

The Influence of the Female Sex Glands on Obesity. — Wagner. (*Zeitschr. ärztl. Fortb.*, **26** : 781, 1929.)

The sex glands predestine certain skin reactions in obesity. Hence a constitution factor is concerned in the existence of obesity. Of 500 women castrated by the roentgen ray method 300 took on weight and of these 200 gained 5 kg. Investigations by Kaufmann have shown that after injection of highly potent sex gland hormone the fat content of the blood is definitely increased, and thus the fatty acid phosphatides are increased; on the other hand, the cholesterin ester is not.

Organotherapy in Neurology. II. Special Report. — Josef Wilder. (*Der Nervenarzt*, **2** : 656, 1929.)

The advantage of synthetic preparations is their totally constant capacity and the entire certainty of dosage; the disadvantage is that they contain not the active, but rather the most active principle for the gland concerned. In substitution therapy the synthetic preparation is often surpassed by the natural gland product (Addison's disease, myxedema).

Adrenalin: There is a widespread opinion that adrenalin is unimportant; this is not true. The author observed very definite effects with doses of 20 drops of a 1:1000 solution or after a tablet, even though they were much weaker than after the same dosage was administered parenterally. Natural products seem to contain hypotensive substances (Roger) particularly the watery extracts. With regard to individual sensitivity it must not be forgotten that the body weight of the patient must be taken into account.

In amyotrophic lateral sclerosis Schacherl emphasizes testis. In arthropathia deformans

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an endocrine subgroup which reacts to ovarian preparations, is certainly present.

In cardiac asthma pituitrin is allowed by many authors.

Angina pectoris should react favorably to administration of parathyroid (Peritz).

Many ovarian preparations were tested in chlorosis. Appert found these ineffective and recommends, on the other hand, the administration of testis to women. Blondel, Marcolango and others reported upon thymus as an effective medium.

Pal recommends and administers very small adrenalin doses, orally, in cardiospasms, especially after mealtimes.

Brünn observed success with posterior lobe of the pituitary in dyspnea and also in cases of cardiac and emphysematous dyspnea. In hypertonia thyroid is recommended by Jagic, Januschke and Molnar. In essential hypertonia Kylin recommends sex gland and the author, too, experienced success with sex gland medication in such cases.

In cephalea of nasal origin adrenalin often gives brilliant results. In myalgic form (Peritz) sex gland therapy and eventually thyroid is suggested.

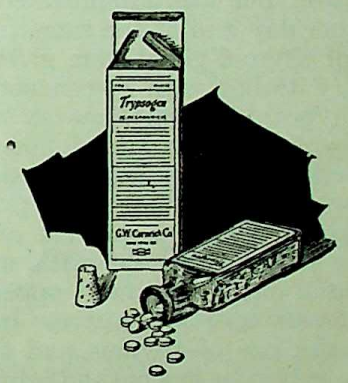
Reports on Post-Operative Treatment. I. Post-Operative Gastrointestinal Paresis and Atony. — Ed. Melchior. (*Der Chirurg*, **1** : 1198, 1929.)

One of the oldest peristalsis-inducing mediums is the hormone derived from the spleen by Zuelzer and Dohrn, which is actually able to exercise a very considerable stimulation on the intestinal tract. Nevertheless, the preparation does not meet with favor because of the occurrence of the usual unpleasant secondary symptoms as evidenced by cold chills and imminent conditions of collapse. The extracts of the posterior lobe of the pituitary form the most active and most applicable substances for the institution of a regular post-operative peristalsis. Their effect extends into the large intestine as well as into the small one. One disadvantage of this preparation lies in the large dosage, wherewith conditions of collapse are likewise imminent. However, the administration of pituitary preparations can not be recommended warmly enough. One important fact is that the action is not restricted to intestinal factors, but also they possess a tonicizing effect on the general circulatory apparatus, one which closely resembles a prolonged adrenalin effect.

The Idea Behind the Product

UNDERLYING the treatment of diabetes today is the conception of a deficient secretion of the pancreas. Experiment and clinical experience have shown that diabetes is a complex disease and not simply due to lack of a single internal secretion. Several internal secretions elaborated by the pancreas as well as the enzyme have been clearly shown to be lacking.

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New Views on Liver Diseases from the Internal and Surgical Standpoint. — P. F. Richter. (*Zeitschr. ärztl. Fortb.*, **26** : 782, 1929.)

The therapy of disturbances of liver function has the task of supplementing the function by means of glycogen administration, in parenchymatous injury the simultaneous construction and fixation of glycogen in the liver must be derived by means of insulin. The chief realm for insulin-sugar therapy is subacute and chronic cases of icterus. Richter recommends relatively small doses of insulin (10 to 20 units twice per day) with the richest possible carbohydrate diet.

Recent Advances in the Therapy of Nervous and Mental Diseases (Exclusive of Fever Therapy). — Alexander Pilcz. (*Wien. med. Wochenschr.*, **79** : 1507, 1929.)

In the treatment of various myopathies investigations with consequently conducted organotherapy, especially in dystrophia muscul. progress. were promising. In males the sex gland hormone was administered three to six times per day and at the same time small amounts of thyroid gland were given. Cases of pituitary tumor with conspicuous symptoms of hypothyroidism likewise had their pituitary symptoms favorably influenced with thyroid medication (for example, disturbances of sight) which is very important practically. In Raynaud's disease a process of thyroid medication in combination with sex gland hormone and pituitary, often appears especially necessary as a preventive. In morbus basedowi the use of thymus and sex gland preparations besides arsenic and bromide may be recommended. In tetany the expectations have not been entirely fulfilled with regard to preparations of epithelial substance. In many tick-forms of adolescent individuals a combined thyroid-sex gland medication brought about very good results. Dosage with other sex gland preparations, however, gives slight success.

In mental diseases with sitophobia insulin injections have proved very effective because the patient is again brought to spontaneous ingestion of food on account of a strong feeling of hunger aroused.

In psychoses of the group schizophrenia organotherapy is capable of accomplishing something in new cases (catatonics and hebephrenous forms) (Kauders). In female individuals with deferred or faulty development of puberty organotherapy causes not only initiation of sex maturity but also cure of the psychosis.

Discussion on the Subject of Alkali Therapy of Acidosis. — Meyer-Bisch (*Zeitschr. ärztl. Fortb.*, **26** : 778, 1929.)

Acid secretion of the stomach and pancreas secretion run parallel. In each case of achlorhydria the pancreas secretion must be treated simultaneously. If the acid secretion must be decreased the ensuing pancreas defect must be simultaneously paralyzed.

Investigations on the Threshold for the Medium Influencing Diuresis with the Help of Intrarenal Injection and Reduction of Kidney. — Hans Molitor and P. Nikoloff. (*Arch. exp. Path. u. Pharmakol.* **145** : 331, 1929.)

The inhibition of diuresis occurs neither more abruptly nor more strongly with intrarenal injection of pituitary extract than with subcutaneous injection.

After subcutaneous injection of pituitary extract the inhibition of diuresis occurs at once, but lasts only for a short time.

Following intracisternal injection of pituitary extract an inhibition of diuresis occurs which is similar to the effect with intravenous application in abruptness and with the subcutaneous effect in duration. For the diuresis-inhibiting effect of pituitary extract in intact and unnarcotized animals there is no evident genuine renal threshold.

On the Effects of Pituitrin and Insulin on the Secretion and Blood Vessels of the Isolated Adrenals. — M. P. Nikolaeff (*Naunyn-Schmiedebergs Arch. exp. Path. u. Pharmakol.*, **140** : 225, 1929.)

The limits of concentration of pituitrin which no longer effects secretion of the medulla substance of the isolated organ are about 1:1,000,000,000. Insulin acts analogously to pituitary substances, only with insulin the secretion is longer taking effect and hence lasts longer. With continuous transfusion the effect ceases. The effect on the vessels consists of a vasodilatation and an additional constriction with pituitrin solutions from 1:1000 to 1:10,000. The insulin blood vessel effect pursues a slightly regular course.

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Concerning the Blood Sugar-Active Substances in Secretin Extracts. — H. Heller. (*Arch. exp. Path. u. Pharmakol.*, **145** : 343, 1929.)

There are contributions which state that the stimulation of the internal secretion of the pancreas may result from one of the hormones sent into the blood from the intestinal wall.

Oehme and Wimmers, Takaye, Zunz and others state that the intestinal secretin has a blood sugar-decreasing effect.

The author made common salt extracts from the intestinal cortex of rabbits and tested their effect on normal and heightened degrees of blood sugar. These extracts lower the hyperglycemia after peroral and intravenous glucose administration and permit the succession of hypoglycemia. Fasting blood sugar was slightly decreased by the extracts. The adrenalin hyperglycemia was influenced in the same way as the alimentary. The active principle of the extract is identical neither with histamin nor cholin. The active extract may be obtained only from the mucous membrane of the duodenum or the upper jejunum. The extract when administered gives a negative biuret and xanthoprotein reaction, Millon weakly positive, Pettenkofer test for bile acids and Gmelin test for bile color negative, Pauly test intensely positive. The substance is stable against cooking, the question of identity with secretin could not be set aside without objection. It was shown that insulin was not contained in the mucous membrane of the upper intestinal tract.

Report on Liver Therapy Particularly in Combined Treatment with Arsenic. — Hans Hollmann. (*Deut. med. Wochenschr.*, **55** : 1834, 1929.)

On the basis of his experiments the author was able to offer a combination of arsenic with liver extract for the treatment of anemia. While arsenic, through stimulating the blood-forming centers increases the production of red blood corpuscles, the liver extract, on account of its detoxicating effect, inhibits the premature disintegration of the formed red blood corpuscles. The indication for introduction of arsenic-liver therapy is not confined to pernicious anemia alone, but may be widely applied; for instance, chronic streptococcus infections, associated with secondary anemia, seem to be favorably affected with arsenic-liver treatment.

Studies on the Mechanism of Adrenalin Glycosuria. — J. E. Holst. (*Zeitschr. klin. Med.*, **111** : 761, 1929.)

Since earlier investigations on the mechanism of adrenalin glycosuria did not give any definite conclusions, the author conducted other experiments on this subject. In 8 test persons (1 normal, 1 case of ulcus ventriculi, 1 case of renal glycosuria, 1 case of morbus basedowi and 4 diabetics) calculations of values were plotted on curves, partly after subcutaneous adrenalin injection and partly after glucose administration. The tests justify the assumption that the mechanism of adrenalin glycosuria is of the same sort as that of alimentary glycosuria.

Inverse Hormone Effects. — G. Katsch. (*Med. Klin.*, **25** : 1723, 1929.)

In repeated intravenous administration of small doses of hormone in short intervals of time, effects may occur which can be deemed the opposite of the recognized proper effect of the hormone concerned. By means of very small doses of insulin the author was able to effect a long continued increase of blood sugar in an animal experiment. The amounts of hormone administered would have induced intense drop in blood sugar if given at one time in one dose. These observations are important but they do not influence the practical therapy of diabetes.

Skeletal Muscle Extract As a Tonicizing Medium. — J. S. Schwarzmann. (*Wien. klin. Wochenschr.*, **4** : 1513, 1929.)

As a result of favorable effects with skeletal muscle extract of the calf in angina pectoris the author tested the influence of this on various other disease conditions such as hypodynamia, in nervous exhaustion, in conditions of fatigue, in reconvalescents after acute infectious diseases, in diseases associated with psychic depression, in impotentia sexualis, in individuals with restricted capacity of the heart muscle and in dyspnea after slight movements, as well as insufficiency of the myocardium with disturbances of compensation.

In all these disturbances the muscle extract exercised a general tonicizing effect in that it greatly increased the capacity of the patients and brought about a state of euphoria.

That the author has met the necessary requirements for the exclusion of the possibil-

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ity of a suggestive effect, need not be especially emphasized.

The effect of the extract was shown in a very pregnant manner in neurotics who complained of a feeling of oppression in the breast and need of air. In cases in which, owing to sluggish heart activity, movements brought about slight dyspnea these conditions were greatly ameliorated with the extract.

However, in patients with very pronounced insufficiency of heart muscle and disturbances of compensation, the general conditions as well as the dyspnea symptoms were greatly improved under the exclusive influence of the extract, without any further therapy.

The objective findings show that heart tonus, particularly weak previous to injection, is often strengthened in a manner not to be undervalued.

In a single case in which the patient received digitalis, there were indications to support the idea that muscle extract administered simultaneously strengthened the effect of digitalis. This, however, is a problem which must have further study.

Calf Thymus and the Maintenance of Carcinolysis and of Blood Formation in Inoperable Carcinoma. — Alois Kittinger. (*Wien. klin. Wochenschr.*, **42** : 1434, 1929.)

From exhaustive investigations the author draws the following conclusions:

1. The capacity of blood serum for the release of isolated carcinoma cells may be increased by means of transplantation of the thymus of the calf or thymus injections, if it has totally disappeared. Yet a lasting condition was never obtained.

2. The thymus substance given is effective when transplanted, or given by injection or by enema.

3. Disturbance of health can thus proceed from or depend upon the decomposition of the albumin molecule.

4. The formation of blood could not be influenced continuously. An eosinophilia was never obtained.

Concerning the Failures of Liver Therapy in Funicular Diseases of Pernicious Anemia. — F. Krause. (*Klin. Wochenschr.*, **8** : 2177, 1929.)

From the four case histories presented it was shown that the number of red blood corpuscles promptly rose to over 3 millions with liver therapy, and in Cases 2 and 4, even over 4 millions. Nevertheless, the nervous symptoms grew worse, particularly in the first and fourth cases the spinal symptoms were so severe that the disease process in the bone marrow looked as though it would be fatal. At the same time, it must be brought out that the general condition of the patients was definitely improved in all cases, with liver therapy, so that there was no question of a severely cachectic, bed-ridden individual.

The Relation between Parathyroid and Thyroid Glands and Skeletal Growth. — V. Lasas and Z. Mozkus. (*Anat. Anzeig.*, 68 : 113, 1929.)

The growth of the skeleton in dogs (in the first month of life) was inhibited by means of total extirpation of the thyroid gland. In instances of coincident removal of the parathyroid the inhibiting effect on the skeletal system was more plastic. The growth in length was particularly intercepted.

Concerning the Administration of Pituitary Preparations in Kidney Diagnosis. — Ferdinand Liebermann. (*Deutsch. med. Wochenschr.*, **55** : 1879, 1929.)

As has long been known, in water tests on healthy individuals pituitary preparations inhibit diuresis during the first hour with a notable rise in concentration. This obstruction to diuresis is to be observed in slight degree of injury to the kidneys, in kidney diseases without kidney insufficiency. The concentration capacity is not so great, however, that the hypophysin test can take the place of the thirst experiment entirely. In cases of kidney insufficiency with hypostenuria the inhibition of diuresis is often lacking, and particularly in associated increase of concentration. The evidence of Kerppola that there are cases of pronounced kidney insufficiency in which the tolerance for hypophysin was to be considered as evidence of the concentration capacity of the kidney requires further proof.

Organotherapy with Spleen in Tuberculosis of the Lungs. — (*Monde méd.*, 38 : 966, 1929.)

In the Hérold Hospital from the year 192[illegible] to the end of March, 1928, twenty-six children underwent spleen therapy. The following results were thus obtained. With regard to weight, in a single case there was a drop. In 3 cases the increase in weight amounted to

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more than 10 kg., in 3 cases to more than 8 kg., in 5 cases more than 4 kg., in 3 cases more than 6 kg., in 2 cases more than 4 kg., and in 1 case more than 1 kg. The bacilli disappeared in 10 cases; they remained in 12 cases, of which one, however, showed an unheard of decrease in number. The roentgen picture exhibited a clearing up in 12 cases, no clearing in 11 others. In all cases in which a blood corpuscle count was made, there was evident a remarkable and permanent improvement in red blood corpuscles. In all cases in which the calculation was made a significant increase in proportion of hemoglobin occurred. Of the children observed there were 12 with evening temperature between 38.6° and 40°, 8 of these were fever-free, 4 exhibited a fall to 38°. As the end-result of 26 cases 4 instances of death were reported, 1 case of exacerbation, 4 improvements, 7 striking improvements and 10 cures, or such an improvement that the patient is considered to be on the road to recovery.

The Feeding of Spleen in Suppurating Diseases of Bone and Joint. — F. Löffler. (*Zentr. Chir.*, **56** : 2946, 1929.)

The author administered a mixture which was given in soup in amounts of about 3 tablespoons per day. Children with very severe tuberculosis were treated, intensely fistulizing bone and joint diseases which had been treated for months previously with other methods.

Locally, cessation of the fistulization occurred. Diminution and reddening of the granulation, cessation of edematous swellings and pressure pains were obtained. The general condition was strikingly improved. Also, children with severe chronic osteomyelitis, in whom well defined sequestration of the bone had not yet occurred, were treated successfully with spleen preparation.

On the Action of a Hormone of the Anterior Lobe of the Pituitary on the Release of Milk Secretion. — F. Grüter and P. Stricker. (*Klin. Wochenschr.*, **8** : 2322, 1929.)

The investigations of the authors on the influence of a hormone of the anterior lobe of the pituitary on the secretion of milk gave the following results. A hormonal substance is contained in the anterior lobe of the pituitary which can exercise a particularly stimulating effect on the mammary glands and which most certainly causes the release of the secretion of milk at the moment of birth. Other organ extracts such as those from liver, lung, posterior lobe of the pituitary and even the placenta have exhibited negative results in this respect, even though they have been given in doses much higher than in the experiment cited. The milk-increasing effect of placenta extracts is often quoted. One of the authors studied this problem in 1920. In cows which were experiencing lactation, whether after bearing or several days after ovariectomy, it was possible to obtain a degree of improvement in milk supply with ingestion or subcutaneous incorporation. However, it seems that the influence of the anterior lobe of the pituitary is more effective. Besides it was never possible to initiate lactation with placenta extracts, and indeed the authors who were able to provoke milk secretion could only do so after many weeks of repeated injections.

Metabolism Experiments in Pernicious Anemia. I. Contribution. Basal Metabolism and Liver Diet. — K. Grassheim. (*Zeitschr. klin. Med.*, **111** : 601, 1929.)

From observations and clinical experiments in thirty cases of Morbus Biermer it follows that very severe disorders of metabolism may be present when an obvious total remission is effected by means of liver diet. Hence one can not speak of an absolute cure with liver diet.

Oral Spleen Therapy in Polycythemia. — U. Friedemann and H. Deicher. (*Klin. Wochenschr.*, **8** : 404, 1929.)

As an outcome of the work of Lichtwitz and Francke the authors report on procedures with a spleen preparation in a case of polycythemia. From their tables it is evident that after administration of spleen tablets the hemoglobin values fell from 95 to 85 and the erythrocyte counts from 6,200,000 to 4,150,000. On the day following the introduction of spleen tablets (29/IX) the hemoglobin values rose again to 97, the erythrocyte count to 5,470,000. In the following table the values also remained high, on the average, and finally reach the initial values observed, again. Unfortunately the authors were unable to make more recent tests of the results of spleen therapy, for the patient left the hospital. In the authors' experiments a definite influence on erythrocyte count and on hemo-

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globin values in polycythemics seems to be presented through spleen therapy.

Date	Hemoglobin (Sahli)	Erythrocyte Count
20/XI/1927	100	5,900,000
21/XI/1927	95	5,600,000
22/XI/1927	110	4,900,000
23/XI/1927	104	5,100,000
24/XI/1927	..	.....
25/XI/1927	..	.....
26/XI/1927	98	4,690,000
27/XI/1927	..	.....
28/XI/1927	95	4,440,000
Spleen tablet medication commenced		
29/XI/1927	85	4,150,000
30/XI/1927	97	5,470,000
1/XII/1927	108	5,600,000
2/XII/1927	97	6,160,000
3/XII/1927	103	5,820,000
4/XII/1927	96	6,250,000

The Diuresis-Promoting Effect of Liver Extract in Dogs with Insufficient Kidney. — Susi Glaubach and Hans Molitor. (*Wien. klin. Wochenschr.*, **42** : 1438, 1929.)

The diuresis-promoting fraction of liver extract is present in a powder which is easily soluble, in cold, in physiological salt solution and has a diuretic effect on dogs in amounts of 1 to 2 mg. per kg. The subcutaneous injection of it is rather ineffective. Secondary symptoms were never observed either locally or generally. Intravenous injection, which was incidentally tested, acted no better than the subcutaneous, and was quite free from secondary symptoms. The blood pressure of decerebrate cats was only slightly depressed with the preparation so that the histamin content of the substance is negligible. The substance is free from bile acids and lipoids and very poor in albumin. Its salt content can not be the cause of the diuresis-promoting effect, for the control tests with the incinerated product were without effect on water metabolism. Only so much of an increase in urine will be derived as there is substance in the liver which could be transferred into the extract. Tests with such a strong purin derivative as theophyllin have often shown that the subcutaneous injection of 0.01 to 0.02 gm., hence an amount 10 to 20 times greater than administered liver extract, remained entirely without effect on the urine.

What the nature, chemically, of the diuresis-promoting substance is, is not yet known. Just as little can be predicted as to why a substance derived from the liver is so effective in an oliguria with genuine renal dependence. It must be remembered, however, that there are a number of older experiments according to which an incretion of the kidneys, Nephrotoxin, formed particularly in atrophying kidney tissue, is capable of injuring the liver specifically, and also the kidney itself.

Whether the diuresis-promoting principle will also be demonstrated in human beings as a useful therapeutic medium in renal and other disturbances of water economy, experiments first must instruct us.

The Influence of the Thymus on Growth under Normal and Abnormal Conditions. — Leon Asher and Pierin Ratti. (*Klin. Wochenschr.*, 8 : 2051, 1929.)

There exists a series of viewpoints on the fact that the thymus has an influence on growth. For the recent investigation of this function, always more and more restricted growth experiments were conducted on very young rats. In the first series animals were fed under optimal conditions. The one series of very young rats received a diet consisting of milk and bread, the other series received the same diet, and simultaneously, at definite intervals, intramuscular injections of thymus extract, and also, thymus was ingested. The growth in the latter series was very abrupt and intense. Hence it was concluded that in very young animals the addition of thymus to the diet, and particularly the parenteral injection furthers the growth process. More significant for the effect on growth, however, are such tests as experiments conducted under unfavorable conditions. For such conditions the rickets diet of McCollum was chosen and the animals were kept in the dark. Two series were arranged. The one, of young rats was placed in a glass chamber (Bern metabolism cage) and received the diet inducing rickets exclusively. The other series received the same diet, but to every three animals collectively, 30 gm. of fresh thymus was also given. Both series were kept away from light. The control series developed a typical severe rickets. The other animals receiving thymus, however, developed in a normal manner. The microscopic investigation which Professor Wegelin was kind enough to do in the thymus animals, presented evidences of normal ri

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and femur epiphyses besides rib fractures. From these experiments it is shown that the addition of thymus can totally offset the effect of a rickets-promoting diet. Whether the thymus gland acts as a substance to improve nourishment or hormonally, further experiments must determine.

Concerning Blood Pressure Disturbances in Morbus Basedowi. I. Blood Pressure Increase and Instability of Height of Blood Pressure. — E. Barath. (*Zeitschr. klin. Med.*, **111** : 718, 1929.)

It is not yet decided what importance is to be ascribed to an increased thyroid gland activity and the change of blood pressure niveau. The expressed juice of the thyroid gland appears to exercise a depressive effect on the blood pressure.

v. Fürth and Oswald have shown that the intravenous incorporation of thyroid gland preparations increases the effect of adrenalin injections. On the other hand Falta and Newburgh, and Nobel and Pilz found a decrease in blood pressure if large amounts of thyroid substances were ingested. The author investigated the changes in the blood pressure curve induced by thyroxin in therapeutic doses, in healthy persons, but could not determine any definite effect of the medium on the blood pressure values. Thyroid ingestion offers no uniform explanation of the conditions of disturbances of equilibrium in the blood pressure system.

Concerning Blood Pressure Increase and Certain So-Called Hypoglycemic Conditions following Insulin Injections. — A. Brems and Cai Holten. (*Bibliothek f. Laeger*, **121** : 463, 1929.)

The authors present experiments for the determination of an alteration in secretion of adrenalin following insulin injections, in normal and diabetic persons.

Rise in systolic blood pressure was observed in normal as well as in diabetic individuals. The increases seemed to occur only in those cases in which "hypoglycemic" symptoms, in the form of vasomotor symptoms, were observed, while in all other cases the blood pressure remained uninfluenced, even though the blood sugar exhibited a very intensive drop.

The rise in blood pressure and the "insulin condition" were in direct parallel. The rise in blood pressure, apparently, is dependent upon adrenalin activity brought about by insulin through the splanchnici with central irritation.

This central irritation is to be traced partly to drop in blood sugar. The hyperadrenalinemia incurred after insulin injection must be influenced by the glycogen-mobilizing effect modifying the insulin-blood sugar effect.

Circulation Hormone and Internal Secretion. — E. K. Frey. (*Münch. med. Wochenschr.*, **76** : 1951, 1929.)

The blood contains large amounts of hormone. On the basis of a clinical finding (operative) the author determined the interrelationship between the internal secretion of the pancreas and the substance found in the urine. After total extirpation of the pancreas the hormone content of the urine is decreased about 80 per cent in a short time. During a 2 hour clamping off of the pancreas blood vessel, the amount of circulation hormone in the urine is significantly decreased, after release of the flow through the organ again it increases. The circulation hormone may be derived from the pancreas tissue in large amounts. From 1 gm. of pancreas substance the author derived 50 units of active substance. Doubtless the hormone is the basis of many other effects, which appear to proceed particularly from the spleen. With removal of the spleen the hormone content of the urine drops off rapidly and intensely. The author assumes that the hormone-activating substance is formed from the lymph glands; by means of 1 gm. of lymph gland 500 units of the circulation hormone can be rendered inactive.

The Nerve Disturbances of Biermer's Anemia and Liver Therapy. — H. Curschmann. (*Med. Klin.*, **25** : 1689, 1929.)

The impression gained from statistics of an obvious accumulation of spinal complications in pernicious anemia following institution of liver therapy is to be directly explained (in part) through success of liver therapy. Previously, the presence and progression of the spinal symptoms were overshadowed by the disease picture of the general state of cachexia. Now, following liver therapy, with a blood finding at least representing a picture of temporary cure, the patient presents an opportunity for the special consideration of the symptoms which can not be influenced with liver therapy. In the failure of liver treat-

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ment in the spinal syndrome of pernicious anemia it would be premature to draw any theoretical conclusions, on the one hand, concerning the premise that liver action is not a vitamin effect, as Stepp has propounded, that on the other hand, liver therapy is only a symptomatic treatment of the blood injury, but not an etiotropic combatant of the cause of the entire disease condition. However, the experiments give evidence of the fact that the funicular myelitis of the Biermer patient requires a particular treatment; if the fever cure treatment is applied here it must be remembered that this therapy, of course, must be instituted only after total compensation of the blood injury is effected with liver preparations.

On the Question of the Pathological Changes in the Internal Organs of the Dog after Introduction of a Spleen Pulp Emulsion into the Blood (Experimental Investigations). — T. Chorunschenko. (*Zeitschr. ges. exp. Med.*, **64** : 185, 1929.)

On the basis of his animal experiments the author comes to the following conclusions.

1. Disintegrating spleen tissue possesses toxic properties.
2. If spleen emulsion be introduced into the blood, a general effect is produced in the organism in the form of a degeneration in all parenchymatous organs.
3. The toxic effect after introduction of an emulsion of spleen tissue is evident equally as much whether the spleen originates from the same or another animal.
4. If the spleen is present in the animal organism, the emulsion introduced has a less harmful influence than after splenectomy. It is possible that the spleen existing in the organism produces substances by means of which the disintegration products of spleen tissue may be neutralized.

Osseous Lesions in a Myxedematous Cretin Dwarf. — Berard. (*Presse méd.*, **37** : 39, Jan. 9, 1929.)

The author reports a case of a man of 39 years, measuring 1.10 meters, with the usual history. The interesting part of the observation is a series of radiographs which show articular lesions and a persistence at certain points of the connecting cartilages. In addition there exist osseous dystrophic lesions which resemble those of fibrous osteitis.

DYSMENORRHEA

The demonstration of the influence of the several hormones of the ovary on menstruation is one of the brilliant achievements of endocrinology. The estrus-stimulating follicular hormone and the inhibiting hormone of the corpus luteum in conjunction with the hormone of the anterior pituitary and of the adrenal cortex form a delicately balanced mechanism controlling menstrual flow, changes in vaginal and uterine mucosa and general metabolism. Slight defects in this mechanism as a whole or of its individual endocrine gland components give rise to irregularities of menstrual process of which pain at the menstrual period is a conspicuous symptom.

In treatment this endocrine mechanism may be stabilized with

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On the Pathology of the Endocrine System. — G. Döderlein. (*Beitr. path. Anat. u. allg. Physiol.*, **83** : 92, 1929.)

Disturbances of the internal secretions, especially functional disturbances of the thyroid gland not only diminish the total value of the sperm cells of an adult individual to total sterility, but they also injure the fetus in the pregnant mother (animal experiments) during the particularly sensitive epoch of embryonal development. This sort of sperm injury in the fetus, however, in the absence of definite morphological evidence of the impregnation capacity or incapacity of the sex germs, first comes to light in the age of sex maturity, as a lack of function. Hence precaution can not be advised too much in the administration of endocrine gland products in pregnancy. Every endocrine therapy which does not serve exclusively to remedy the existing insufficiency of internal secretion causes a disturbance of the equilibrium. Mother and child are a biological unit. Growth regulating hormones, to which the thyroid gland hormone also belongs, act on the fetal organism in its initial development much more intensively than on the adult body of the mother. Whether harm ensues, or whether the endocrine disturbance can be smoothed out without trace is merely a question of degree of disturbance in the experiment, and with therapeutic administration, a question of dosage. For the assay of natal endocrine disturbance, however, the phenotypic appearance alone is not sufficient. The endocrine system only assumes its full function after puberty, when the sex glands are incorporated. With regard to the full value of these, however, only the genotype evident from the generations decides the probability above all of a latent injury.

On the Treatment of Diabetes Insipidus with Pituitrin and Vasopressin in Endonasal and Subcutaneous Administration. — A. W. Elmer and M. Scheps. (*Münch. med. Wochenschr.*, **76** : 1917, 1929.)

Pituitrin as a snuff powder has a favorable effect on diabetes insipidus and should be considered the method of choice.

The endonasal administration of pituitrin as snuff powder requires larger dosage than the subcutaneous application. The endonasal treatment is to be preferred over the injection method, not alone because of agreeableness, but also because of the long lasting pituitrin resorption and the avoidance of unsatisfactory secondary symptoms resulting therefrom (increased blood pressure and anuria).

The endonasal administration of pituitrin snuff powder is to be preferred to pituitrin tamponade treatment, since the latter requires more technique, the tamponades must be changed every six hours in order to avoid irritation of the mucous membrane, and pituitrin in tamponades is more difficultly resorbable and requires greater dosage. Vasopressin injected subcutaneously acts more strongly than pituitrin, but causes unsatisfactory accessory symptoms: body weakness, headache and stomach ache, nausea and diarrhea. Vasopressin treatment by means of tamponades is not suitable for long treatment.

In endonasal treatment with vasopressin no secondary symptoms appear.

Blood Sugar-Decreasing Extracts from Human Organs. — H. Brugsch. (*Zeitschr. ges. exp. Med.*, **65** : 574, 1929.)

The investigations in dead organs for their insulin content must be performed with the consideration that these can quickly deteriorate after death, and particularly the pancreas. The values found decrease greatly and appear to be especially dependent upon the state of nutrition. Thus, the pancreas of an individual dead from starvation contains no insulin, while the musculature and heart are still rich in content. In the main, the collective musculature contains much more insulin than the pancreas, whereas the liver, spleen and kidneys contain as much or less.

Comparative Experiments on the Activity of Synthetic Thyroid Gland Preparations. — Lisbeth Auerbach and Béla Klein. (*Klin. Wochenschr.*, **8** : 2332, 1929.)

Much has been done on the subject of the effect of thyroid gland preparations in healthy persons. Unity of opinion on the question has not been reached as yet. While the opinions regarding native preparations are in accord, for, one can, even if not in all cases, at least with a normal amount of surety, call forth hyperthyroid symptoms until thyrotoxicosis is attained, the reports concerning pure thyroxin and on its effect on the organism read very variously. Experiments were made with preparations from different manufacturers and the activity was tested with regard to weight tables, diuresis curves, metabolism and basal metabolism. In gen-

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eral, then, a result was noted with subcutaneous and intravenous application methods which was quite variable only quantitatively. But with peroral dosage there were extensive divergences, in that one series of investigations gives contradictory results concerning their activities, or gives evidence of a minimal effect; another, however, affirms them and partly coincides with the above mentioned processes.

For the first test series which was assayed with preparations from other concerns the authors investigated thyroxin in the form of ampoules and drops, and were able to confirm a definite thyroid gland effect in the organism. A parenterally administered dose of 3 times 2 mg. approximately agrees with double the amount of ingested thyroxin. The authors will report further, in another place, concerning the other test series, and on the literature up to the present time.

Insulin, Synthalin and Glukhorment. A Comparative Investigation concerning Their Effect on Glucose Fixation through Cells. — E. Salén and T. Nyrén. (*Acta med. scand.*, **69** : 69, 1928.)

An investigation was made to determine whether the action of insulin in increasing glucose fixation, noted by the Graz School, in the blood cell experiment, is a specific effect for insulin. The experiments carried on by the authors with synthalin and glukhorment under similar experimental conditions show a qualitatively identical effect in increasing glucose fixation for these two substances as for insulin.

It is to be assumed that this effect is entirely conditioned by the synthalin-like substance present in glukhorment. This effect in increasing glucose fixation belongs also to the chemically pure substance, synthalin.

The proof that synthalin *in vitro*, even in a completely insulin-free medium, exerts an action in increasing glucose fixation which harmonizes with that of insulin seems to suggest that synthalin has a direct and primary effect on sugar regulation.

The Action of Insulin on Regeneration. The Biological Rôle of Potassium and Calcium Ions in This Process. — B. A. Schazillo and M. Ksendowsky. (*Pflügers Arch. ges. Physiol.*, **220** : 774, 1928.)

The experimental results of the authors support the favorable action of insulin and calcium ions on the formation of callus. Fro Repinous and Leberts' investigation it ma be seen that insulin introduced into the bod effects a shifting of the acid and base equi ibrium towards the side of the acids. Throug this shifting callus regeneration is promote (according to Abderhalden). On the oth hand, introduction of calcium incites the ce tral stimulation of the vagus nerves, whic increases insulin production in the pancrea From this it may be concluded that insuli (as pancreas internal secretion and insulin like substances present in the body fluid combined with potassium and calcium ion not only plays an important biological rô in the transformation of substances, but also in the formation of structure elements. At any rate it may be gathered from the resul of the authors' experiments that insulin whe it is introduced into the body, increases bon regeneration.

Concerning the Action of Hormones, i Particular of Pituitrin on the Vasomot Centers. — Ch. Inalea. (*Zeitschr. ges. ex Med.*, **63** : 523, 1928.)

The author was able to corroborate th finding of Spiegel and Saito, that the injectio of doses (0.1 to 0.2 cc.) of pituitary extrac inactive intravenously, into the lateral ve tricle in rabbits, may cause a slight fall blood pressure, concerning which, howeve it must be emphasized that the action pituitary preparations is exceedingly inco stant. The author's experiment speaks favor of the idea that the pituitary product its way through the ventricle in the subarac noid space rather exerts a slight action on t diencephalon center in the sense of the inci ment of a vasodilation, whereas it scarc seems to influence the rhombencephalon ce ters.

Hemorrhage following Delivery: Me ical Treatment. — Varon and Chave (*Bull. obstét. et gynécol.*, No. 9 : 869, 1928.)

In a patient with spontaneous delive which was terminated within 40 minutes a with apparently, absolutely complete placen an abundant hemorrhage suddenly appear on the fifth day following delivery. In ad tion to hot vaginal irrigations, subcutane injection of post-pituitary extract was ma and calcium chloride was administered int nally. On the following day another he orrhage. No more hemorrhage followed; t patient was discharged cured after 12 days

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Hemorrhages in the Menarche. — F. Kermauner. (*Wien. med. Wochenschr.*, **78** : 1511, 1928.)

Hormone treatment strives for a causal attack with the ultimate end of a cycle regulation. The author tested a great number of the procedures proposed with patience and perseverance. He tried treatment in the form of oral administration and of injection intravenously and intramuscularly. The author was unable to determine any great differences in the manner of action of the various ovarian preparations on the market. They were all useful in certain cases and all failed in more severe cases. In milder cases a trial of one of these remedies is indicated. In the future the author will use only a treatment with ovarian preparations by mouth, in the form of suppositories or at any rate through administration of intramuscular and subcutaneous injections; in no case, however, will he choose the intravenous route. The author also hopes to obtain better results when more active preparations are at his disposal than at the present time. On the other hand, in cases of hyperthyroidism, a truly causal administration of thyroid tablets or thyroxin or small doses of iodin is instituted. Among the remedies for symptomatic therapy the author counts blood transfusion, calcium and pituitary preparations in treatment of these hemorrhages.

A Case of Pituitary Infantilism. — G. Roussy, J. Bollack and Kyriaco. (*Presse méd.*, **37** : 21, Jan. 5, 1929.)

The authors present a case of pituitary infantilism where the early visual symptoms drew attention to the disorders of development. The patient was a child of 12 years, of very well developed intellect, presenting height, weight and dentition of a child of 7 years, despite the existence of normal points of ossification for his age. The sella turcica is very much enlarged but the clinoid apophyses were respected. Vision of the right eye, which had been failing for the past 2 years, had become almost negative and the papilla was atrophied. Vision of the left eye was normal despite very definite temporal narrowing of the visual field. There were no signs of intracranial hypertension nor of diabetes insipidus nor of adiposogenital syndrome. The authors come to the conclusion that it is a case of pure infantilism of pituitary origin, of Souques and Chauvet's type, due probably to an intracranial tumor.

Endocrine Preparations. — Schemensky. (*Münch. med. Wochenschr.*, **75** : 1783, 1928.)

In various endocrine disturbances (at the climacteric, in pluriglandular infantilism, in endogenous obesity and male castration) the author was able to obtain favorable clinical results with fresh substances of the glands in question (testis - ovary) as well as with the corresponding endocrine preparations.

The Search for Adrenalin in the Suprarenal Capsules, post Mortem. — L. Langeron and P. Lohéac. (*Rev. franç. endocrinol.*, **6** : 347, Oct., 1928.)

The search for adrenalin in the suprarenal capsules has but a speculative interest. Physiology teaches us that suprarenal extracts are hypertensive and the recent works of Tournade and Chabrol have shown the rôle of the suprarenal secretion of adrenalin in the maintenance of arterial tension.

The authors have undertaken their investigations in order to determine what contribution the search for adrenalin can bring to this theory: Whether there is a relation between the tension observed during life and the rate of adrenalin in the suprarenals after death; under what conditions and by what technique should this research be practised in order that the results be as certain as possible.

The authors conclude that in order to ascertain exactly the amount of adrenalin in human suprarenals these organs must be removed as rapidly as possible after death, 2 to 3 hours at the most and they must be placed in the sulphuric vacuum as soon as possible. The dosage should take place after 24 hours in the vacuum. Dosages which are not made under these conditions have no great value, for the absence of adrenalin in the suprarenals at autopsy may be due to the influence of cadaverization. Moreover, an examination of the suprarenals removed very soon after death would give only the amount of free adrenalin and not the amount of total adrenalin.

The results of authors, who have practised these dosages under defective conditions can not be retained. Of course, the rapidity of death certainly influences the amount of adrenalin in the suprarenals. The results are, however, at least comparable among themselves. At the present time, in the absence of a great number of dosages effected under these conditions, it is impossible to know whether there is a constant relation between

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the amount of adrenalin of the suprarenals and the tension observed during life.

The precise conditions under which such researches should be instituted are not such as to render them very frequent or very easy. One does not often have occasion to make autopsy on patients with hypertension. Thus, in two patients with hypertension, whose vasculorenal apparatus was sufficiently healthy for the hypertension to be considered solitary or essential, and who died rapidly of cerebromeningeal hemorrhage, the authors found the amount of adrenalin to be 0.39 gm. and 0.06 gm. per 1000 gm. of gland, and this same amount (0.39 gm.) was also found in a cachectic tuberculous patient with hypotension. It would, therefore, be premature to draw conclusions. However, the authors found an interesting indication which again brought up the question of the relations between arterial tension and suprarenal adrenalin, in the following fact: Of two suprarenal tumors, one hypertensive and the other with normal tension, the first was found to be especially rich in adrenalin, while the second was entirely deprived of it. The observation is not unique and more precise indications on the subject may be found in Lohéac's thesis, etc. If, therefore, in a general way it is admitted that neoplastic tissues possess to an exaggerated degree the properties of the elements from which they have issued, the condition favorable to the study of these phenomena may be found in this exaggeration itself.

However it may be, the search for adrenalin in the suprarenal capsules, *post mortem*, is capable of giving results which appear to be interesting, but only under the technical conditions enumerated in this article.

Regarding Edema of the Face at Menstruation Time, of Endocrine Origin, in a Heredosyphilitic. — J. Gaté and J. Rousset. (*Presse méd.*, **36** : 1481, Nov. 21, 1928.)

The patient, an Algerian, aged 27 years, menstruated normally at 11 years and became amenorrheic at 18 years. Her menstrual periods are characterized by discomfort and very marked facial edema, accompanied by sensations of burning, and lasting 5 to 6 days. Her urine was normal. The various functional tests of the endocrine glands revealed a definite hypothyroidism with dysthyroidism and sympathicotonia which become exaggerated at the time of menstruation. This patient is an hereditary syphilitic. Thyro-ovarian treatment associated with arsenobenzol caused t discomfort to disappear, in particular t menstrual edema.

Pituitary Dwarfism. — Lucke. (*Münc med. Wochenschr.*, **75** : 1783, 1928.)

In a 6 year old child with pituitary dwar ism the author was able to obtain a very goo growth-furthering effect by anterior pituita therapy continued for a long period of time.

The Hormone of the Female Se Glands. — F. Siegert. (*Med. Klin.*, **24** 1479, 1928.)

The hormone production in the ovary i at its height immediately before and during menstruation. The production sites are no only the maturing follicle and the corpus luteum but also the cells of the theca interna In pregnancy, the hormone formation is stil essentially raised but is, however, manage only in small part by the ovary and in larg part by the placenta. The action of the se gland hormone is not species specific but se specific, that is, it extends only to the genita zone. Although the hormone certainly effec the setting in action of the growth effect, th growth stimulation does not extend to the se glands. It is neither possible to bring abou an enlargement of the ovary nor the matura tion of a follicle through the estrous hormon On the contrary, the maturation of the follic is inhibited by the hormone. The very note worthy property of the hormone is its abilit to restrain the male sex function. In this cas it is not merely a temporary cessation o spermatogenesis, but also a retrogression o the testis, penis, prostate and seminal vesicle

Portion of the Pituitary and of th Hypothalamus in Experimental Diabete Insipidus. — P. Trendelenburg. (*Klin Wochenschr.*, **7**: 1679, 1928.)

Following removal of the pituitary a n inconsiderable amount of a substance appear in the tuber cinereum, which acts on the excr tion of urine in a similar manner to that of th posterior lobe of the pituitary, and which present in the tuber cinereum of normal an mals in but slight amounts. (It is likewis the same with a uterus-stimulating substance Diabetes insipidus is possibly of pure ho monal nature: when the delivery of the urin inhibiting substance in the posterior pituitar lobe is lacking, the tuber cinereum enter vicariously, and only after its destruction do

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the maximal, no longer reparable diabetes insipidus develop. This theory explains in entirely satisfactory manner all hitherto irreconcilable results of experimental diabetes insipidus in animals.

Influence of the Glands with Internal Secretion on Bone Metabolism. — Stracker. (*Med. Welt*, **2** : 1544, 1928.)

The author used the Abderhalden reaction in diseases which are associated with atrophy, and in arthritis he observed increased decomposition of thymus, parathyroid and ovary. These are, for this reason, therapeutic organ preparations.

Rosacea and Its Treatment. — O. R. Stein. (*Wien. klin. Wochenschr.*, **41** : 1382, 1928.)

The rosacea zone of the face in the female sex is under the influence of the genital sphere. During menstruation the sexually mature woman inclines to outbursts of rosacea, which may become stabilized with the appearance of the menopause. It is, therefore, logical to treat post climacteric rosacea (whose genesis is certainly to be attributed to the disturbed ovarian function) by administration of ovarian preparations and to control the active hyperemia of the climacteric as well.

The Function of the Spleen in Healthy and Diseased Organisms. — R. Siebeck. (*Zentr. Chir.*, **55** : 2324, 1928.)

It has been observed at various times that the resistance of the red blood cells increases following extirpation of the spleen. In any case it may not be mistaken that loss of the spleen signifies a marked stimulation for the bone marrow. It has been assumed that the abolition of some hormone inhibiting the bone marrow, perhaps of the sinus endothelia, asserts itself here. Otherwise also, observations have been undertaken in support of the assumption of special spleen hormones. That the spleen cooperates in digestion is admitted; Schiff has conjectured that the spleen is involved in the formation of trypsin. A pepsinogenous function of the spleen was especially maintained by Tarulli and Pascucci. Other authors refer to a peristalsis-furthering hormone in the spleen. Perhaps these effects are to be explained (Bayer and F. Schulze) by a hormone of the spleen affecting the autonomic nervous system, the vagus. A report is also made concerning the relations of the spleen to other hormonal organs, to the thyroid, thymus, sex glands, etc.

The Influence of the Chronic Administration of Insulin on the Suprarenals in the Rabbit. — H. Langecker. (*Naunyn-Schmiedebergs Arch. exp. Path. u. Pharmakol.*, **134** : 154, 1928.)

The suprarenals of rabbits chronically treated with insulin are on the average heavier than in the normal animal. This applies as well to the absolute value as to the living weight per kilogram. The differences are great enough for the assumption of the origin of a chronic suprarenal hypertrophy through chronic administration of insulin, with due regard for the standard deviation. The adrenalin content which is to be determined colorimetrically is unchanged, so that it may be assumed that the reducing elements of the suprarenals, which are genetically related to adrenalin, may in no way be influenced. The hypertrophy of the suprarenals which arises in the course of chronic insulin treatment in rabbits is largely to be attributed to the cortex.

Treatment by Ovarian Hormone of a Case of Scleroderma. — P. Harvier and A. Lichtnitz. (*Paris méd.*, **18** : 483, Dec. 1, 1928.)

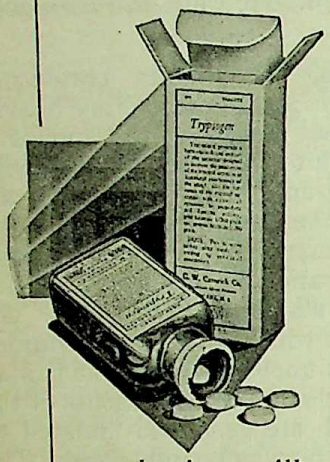
Among the numerous theories seeking to explain the pathogenesis of scleroderma, the endocrine-sympathetic theory is the most frequent. The thyroid, suprarenals and pituitary have successively been held responsible according to whether the scleroderma was associated with or followed goiter, myxedema, exophthalmic goiter, various pituitary syndromes, or coincided with cutaneous pigmentations attributed to a disturbance of the suprarenal functions. A number of authors have observed improvement in their patients following thyroid, pituitary or combined organotherapy. The possible rôle of ovarian insufficiency in the genesis of scleroderma has almost always been relegated to the background.

However, the observation which the authors report is that of a young girl affected with scleroderma of progressive evolution, associated with menstrual disorders and which though not influenced by thyroid and pituitary therapy, was rapidly ameliorated, if not cured, by ovarian organotherapy. The scleroderma had not passed the sclero-edematous

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stage, and was limited to the cheeks, neck, arms, thorax and upper part of the abdomen. Occurring in a girl of 23 years, coinciding with signs of ovarian insufficiency, an evident amelioration followed injections of ovarian hormone.

Although various authors mention ovarian insufficiency in the course of scleroderma, the majority of authors seem to deny it the primary rôle and consider it as a consequence of other endocrine lesions, in particular thyroid lesions. In the authors' patient, there was no sign of hyper- or dysthyroidism. On the contrary, the menstrual disorder appeared from the installation of the scleroderma and has persisted after it. After successively trying without result acetylcholine, pituitary and thyroid organotherapy without observing the slightest local change, the authors had recourse to ovarian organotherapy because of the retardation of menstruation which appeared in the first month following the onset of the scleroderma. It must, accordingly, be recognized that ovarian organotherapy employed alone caused a rapid regression of the cutaneous affection.

The Therapy of Acne Vulgaris. — G. Stümpke. (*Zeitschr. ärztl. Fortb.*, **25** : 69, 1928.)

In cases of acne vulgaris which are related to a dysfunction of the thyroid, the application of ovarian preparations is recommended by Dóczy. In this respect favorable and unfavorable reports appear in the literature. The author himself observed a brilliant result in a 16 year old girl with unusually obstinate acne of the face, following 7 weeks of treatment with one ovarian tablet three times daily and later 4 tablets three times daily, finally with injections of ovarian hormone, which, however, was later weakened by a relapse. In a second case, the complete retrogression of a severe, disfiguring, infiltrating acne of the face was obtained in a 17 year old patient following 15 injections of pituitary extract and no relapse occurred during further observation for several years. In a 25 year old patient with disfiguring affection of the face and raised metabolism, treatment with Antithyroidin Moebius effected a cure. The author has had little experience with combined preparations and considers the administration of single endocrine substances — when an indication to combined therapy is present — more to the purpose.

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The fact of the appearance of acne vulgaris during the period of development, its coincidence with irregularities of the internal genital organs, the observation of slight sexual needs in these patients, simultaneous change of other endocrine organs (thyroid, suprarenals), observations concerning the calcium content of the blood and anomalies of the hair, point to changes in the whole organism and for this reason require a corresponding therapy.

Investigations concerning the Action of Alkaloids Similar to Adrenalin: Ephedrin and Synthetic Ephedrin.—L. Takács. (*Wien. klin. Wochenschr.*, **41** : 1375, 1928.)

The alkaloids, ephedrin and synthetic ephedrin (whose activity is not lessened by oral administration) raise the blood pressure similar to adrenalin. The rise in blood pressure lasts much longer than that induced by adrenalin and is a result of contraction of the vessels, which is conditioned by the stimulation of the peripheral sympathetic nerve endings. The evacuation of the stomach is delayed by ephedrin and synthetic ephedrin. The influence on the gastric secretion is dependent upon the state of equilibrium of the vegetative nervous system and renders possible the ascertainment of a rise in tonus of the parasympathetic system. Therapeutically, ephedrin has been used successfully in the abortion of and prevention or alleviation of asthma attacks and for the relief of bronchial dyspnea.

Joint Disease and Sex Glands. — J. Wiesel. (*Wien. klin. Wochenschr.*, **41** : 1425, 1928.)

Genital disturbances have been described by various authors in acute joint rheumatism, such as cessation of menstruation, exacerbation during menstruation, etc. In girls whose puberty shows rather a hypothyroid course, a pubertal arthropathy is found. These girls also exhibit disturbances of the equilibrium of the endocrine glands, such as severe accumulations of fat through ovarian hypofunction, acroparesthesias, etc. Pains in the joints are also to be observed during puberty in the forms which can be designated as hyperthyroid. Clinically, the course here is somewhat similar to that in the climacteric. A considerable number of authors have described the exceedingly frequent occurrence of chronic deforming arthritis in the climacterium. Roentgen findings, which are in some degree characteristic, are found in particular in the second form of the climacteric, chronic, deforming joint diseases, Heberden's nodules, concerning whose endocrine cause scarcely a doubt any longer exists. Similar pictures can be experimentally produced following removal of the sex glands.

Treatment of Pernicious Anemia with Liver Substance. — C. S. Engel. (*Med. Welt*, **2** : 1644, 1928.)

The property of the liver as exclusive blood forming organ for the red blood cells in the embryonal period induced the author to recommend and use already 3 decades ago embryonal and fetal livers of mammals as remedy in severe anemias.

Such a preparation must contain the nuclein organically combined in the nucleus and phosphorus in similar organic combination, since the bone marrow always produces only erythrocytes with nuclei. It is important that the liver with a lecithin content of 2.1 per cent is a substance richest in lecithin in the body next to egg yolk. Liver appears, accordingly, especially suitable to rebuild the stroma, that is, the supporting substance of the erythrocytes. The statement that the extract of liver substance, furthering the building up of red blood cells, is free from lecithin and lipoids, does not seem suitable to the author. Engel considers it as necessary in the first place to introduce substances of various types into the organism, if the bone marrow is to be stimulated to blood formation in increased degree.

Experiments with Antithyroidin Moebius in Post-Operative Tetany. — A. Zaloscer. (*Med. Klin.*, **24** : 1344, 1928.)

The existence of a functional relation between thyroid and parathyroids can be designated as proved; also from positive observations the conclusion is justified that the hormones produced by both glands are antagonistic to each other. Walbaum and Rudinger assume that the favorable action of Antithyroidin in exophthalmic goiter is to be attributed to a large content in parathyroid hormone, which opposes the pathological increase of thyroid function. If this theory is correct, a direct substitution therapy must be possible with Antithyroidin, that is, this must also prove to be effective in post-operative tetany following strumectomy. Pro-

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ceeding from this consideration, the author gave Antithyroidin in two cases in which pronounced tetanic manifestations appeared following struma operations. In both cases a positive objective result was effected through treatment with Antithyroidin Moebius.

General Viewpoints in the Treatment of Diabetes Mellitus. — T. Weihs. (*Münch. med. Wochenschr.*, **75** : 1764, 1928.)

The author recently had a patient under treatment who showed such a marked cutaneous reaction to insulin that the further treatment with insulin became impossible. Change of the preparation and intramuscular injection did not alter it in the least. Nevertheless, untoward effects of insulin seldom appear and insulin represents a valuable enrichment of diabetes therapy. Of course, there are a series of preparations which are said to influence diabetes favorably, all of which however, can not replace insulin. Synthalin is to be mentioned as being undoubtedly active. It lessens polyuria, lowers blood sugar and in the easy dosage of 20 to 40 mg. causes the disappearance of 20 to 40 gm. of sugar from the urine. The secondary effects are, however, underestimated. It is obviously not a question of dyspepsias but of pronounced toxic manifestations. The longest period of toleration for synthalin which the author has observed amounted to 4 months. Staub also gave a very unfavorable judgment concerning synthalin at the last congress on metabolism. The new remedy, Glukhorment, is only an imitation of synthalin. Fornet's insulin pills to be taken orally are, in the opinion of competent authors and in the author's personal opinion, inactive. The substances present in several plants (garlic) which lower blood sugar, have so slight an effect that too large amounts of the substance concerned would be necessary.

Concerning Regulatory Processes in Experimental Hyperthyrosis. — J. Abelin and R. Vuille. (*Endokrinologie*, **2** : 248, 1928.)

In experimental hyperthyrosis in animals, prophylactic measures of the organism assert themselves at the same time with the metabolic lesions. These measures are aimed at directing the abnormal course of the metabolic process again into physiological paths and to counteract the rise of the resting metabolism, the excretion of nitrogen and the specific dynamic action. This becomes esp cially distinct in sugar metabolism. T latter suffers great changes under the infl ence of the first feeding of thyroid substan in that the glycogen-forming ability of t liver is completely lost while that of t muscles is lost to a certain degree. Th severe attack on the carbohydrate metab ism leaves, however, a considerable protecti against a repeated similar injury. With lat repetition of the administration of thyro substance, the liver no longer loses its abili for glycogen synthesis and the glycogen for ation in the musculature remains normal.

Pituitary Posterior Lobe Extract Actio on Fat Metabolism and the Vegetati Nervous System. — W. Raab. (*Zeitsch ges. exp. Med.*, **62** : 366, 1928.)

The fall of the value for the petroleu fraction in the blood regularly caused b pituitrin is dependent upon a lowering of th neutral fat content in it. This pituitrin effe is weakened by ergotamin or removed b atropin; on the contrary, not essential harmed. Ergotamin and atropin in the selves show no characteristic influence on th blood fat content. The influence of pituitr on fat metabolism proceeds by way of th tuber cinereum — cervical spinal cord — sy pathetic — liver.

Contribution to the Study of th Resuscitation of the Heart and Respir tion in Severe Narcosis Incidents. — Ronzini. (*Policlinico, Sez. Chir.*, **2** : 1928.)

The favorable adrenalin effect in such cas can be supplemented with success by t vagotropic atropin action, since atropin mak it possible for the amphotropic adrenalin produce an exceedingly energetic and pure sympathetic action through suppression of t vagus function. Through addition of pit trin the elective stimulating effect is exert on the cardiac muscle fiber and in order induce respiration, lobulin can be added wi advantage.

Calcium Investigations in Skelet Diseases. — Barrenschien and Gold. (*Wie med. Wochenschr.*, **78** : 1340, 1928.)

The parathyroid hormone prepared by C lip effects an essential rise in blood calciu and an increase in calcium excretion throu the urine. Large doses of parathormone le

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to the typical disease picture of hypercalcemia, in which the experimental animals die in a comatose condition with abnormally high blood calcium values. The action of the parathormone must thus be conceived as a mobilization of the calcium deposits from the tissues. The picture of osteitis fibrosa generalisata of Recklinghausen shows an extensive agreement with the experimentally established inundation of the organism with the hormone of the parathyroids.

Concerning Recent Researches on the Action of Post-Pituitary Preparations and Their Significance in Practice. — A. Leimdörfer. (*Wien. med. Wochenschr.*, **78** : 1197, 1928.)

Following an intravenous injection of pituitrin a rise in blood pressure occurs. Following injection of pituitrin there results a retention of water, an increased condition of swelling of the tissues and thereby a diuresis inhibition, a decrease of water excretion through the kidneys. Pituitrin administered intravenously is often accompanied by good results in post-operative or peritonitic intestinal paralysis. Through its diuresis-inhibiting element, pituitrin renders valuable services in certain disturbances of circulation, namely in attacks of cardiac asthma or pulmonary edema. Injected subcutaneously or intravenously, (1 cc.) pituitrin can frequently be of great service, improve severe attacks, remove danger to life for the moment. Since, moreover, pituitrin is a highly active agent by intralumbar use to influence the blood pressure center directly and so induce a rise in blood pressure from the center, one will endeavor to raise this central fall in blood pressure through intralumbar injection of a good pituitrin preparation in certain disease conditions in which a central fall of blood pressure occurs. In this respect, acute infectious diseases, peritonitis, etc., come into consideration.

Also in lumbar anesthesia a fall in blood pressure can probably be prevented through prophylactic dose of a pituitrin preparation.

Cure of Five Cases of Exfoliative Erythroderma. — Paul Unna, Jr. (*Dermatol. Wochenschr.*, **87** : 1317, 1928.)

In his method of treatment the author proceeded from the standpoint that it might be possible to remove most of the symptoms of the severe disease through easing the peripheral vascular system. He found support in the experiences which have been had with adrenalin treatment in acute toxic dermatoses (Salvarsan and mercury dermatosis). The principal value was placed on the unburdening of the heart and the influence on the peripheral skin vessels. The incisive action of adrenalin salve was especially shown in one case in which an attempt was made to reduce the adrenalin content of the preparation because of the high costs. The favorable action disappeared with the lowering of the adrenalin dosage and returned again with renewed increased use of adrenalin. The author is of the opinion that it will be possible to influence favorably most severe cases of pityriasis rubra Hebrae also through this adrenalin treatment. By this means a considerable advance might be obtained in a hitherto almost hopeless field.

Concerning the Surgery of the Parathyroids. — Westhues. (*Münch. med. Wochenschr.*, **75** : 1618, 1928.)

Transplantation of the parathyroids has little prospect of success. Blum's protective diet (without meat, rich in milk and hemokrin tablets) surpasses all former methods in activity. The author reports concerning several cases of parathyrogenous tetany and a case of the most severe exophthalmic goiter which could be influenced only by Blum's protective diet.

The Measures for Stimulating Peristalsis. — K. Vogel. (*Klin. Wochenschr.*, **7** : 1695, 1928.)

Preparations of the pituitary are recommended for sluggishness of the intestines. The same preparations are first used to induce contraction of the uterus, above all, in weak labor pains. The pituitary products belong to the hormones, therefore, to the substances which are formed in definite organs, frequently in the endocrine glands, reach the blood and lymph passages and excite special physiological processes in cells and tissue. These hormones act as regulators of the circulation as well as of the vegetative and cerebrospinal nervous apparatus and of the metabolism, as "self regulation of the living substance." Cholin, which acts characteristically even in very marked dilution, especially may be designated as genuine hormone of intestinal movement and of the smooth musculature. According to all reports medica-

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ments prepared from the pituitary seem, therefore, actually to exert a stimulating action on the intestine, especially in post-operative paralysis; however, according to Trendelenburg, all are not reliable.

Pituitary and Epilepsy. — E. Redlich. (*Fortschrit. Med.*, **46** : 1083, 1928.)

Even though epileptic attacks are not observed so frequently in pituitary disease as in diseases of other endocrine glands, as for instance the female sex organs, the thyroid and the suprarenals, yet a whole series of cases favor the opinion that definite relations exist between epilepsy and the pituitary and that this gland has an undoubted significance for the general pathology of epilepsy. Up to the present, we are not in a position to fix the exact limits of those forms of epilepsy in whose pathology the pituitary plays a dominant rôle. Consequently, at the present time we can not make any definite statements regarding the administration of pituitary preparations in epilepsy.

A Case of Quincke's Edema following Insulin. — A. Neumann. (*Wien. med. Wochenschr.*, **78** : 1363, 1928.)

The problem here is the appearance of Quincke's acute, local edema following an injection of insulin. To be sure, this phenomenon was not called forth by the insulin itself but by protein substances, the complete removal of which is desirable. Moreover, an individual supersensitiveness of the patient may have played a rôle.

Concerning Synthetic Ephedrin in Urticaria. — W. Frânkel. (*Med. Klin.*, **24** : 1773, 1928.)

The author had the opportunity to test ephedrin medication in a severe case of urticaria. The therapeutic effect obtained was an excellent one. The superiority of the synthetically prepared ephedrin over the more strongly acting adrenalin was also shown in this case, especially in the possibility of oral administration. Moreover, the lack of disagreeable secondary effects (which are frequent with adrenalin and also with ephedrin) was felt to be especially agreeable.

The Chemistry of the Hormone. — G. Barger. (*Ergebn. Physiol.*, **27** : 780, 1928.)

Barger gives a very successful review concerning the status of our chemical knowledge of the hormones at the present time. H begins with adrenalin and follows with th roxin, the two sole hormones with which o can now work with chemical formula. Insuli follows, in which at least the crystalline stat of the product has been reached through th works of Abel and his associates. Short paragraphs concerning the hormones of th posterior pituitary lobe and the anterior pitu tary lobe, of the ovary, of the placenta an corpus luteum, of the parathyroid and cor cerning secretin follow. Finally, the blood forming substance of the liver and the sub stances of doubtful hormone nature (such a gastrin, histamin, cholin, carnosin and sper min) are briefly described.

Concerning the Treatment of Diabete Associated with Pulmonary Tuberculosis — M. Labbé, R. Boulin and L. Justin-Besan çon. (*Presse méd.*, **36** : 1618, Dec. 19, 1928.)

The authors recall that rapidly evolvin bilateral tuberculosis is a frequent complica tion of diabetes, especially serious when i occurs in the course of diabetes with denutri tion.

They report the case of two patients treate by bilateral pneumothorax. Both have bee under treatment for the past 3 years fo diabetes.

In the first case, the evolution of the tube culosis has been followed since July, 192 Treated by a right pneumothorax in Octobe 1927, the patient underwent a left pneum thorax in October, 1928. In the other patien insufflation of the right side practiced i October of this year was followed 1 mont later by insufflation of the left pleura. Th authors direct attention to the excellent tole ance of the patient to bilateral pulmonar collapse.

The conclusions which the authors dra from these observations, though provisiona concern the evolution of the diabetes, the general condition, and the development of th tuberculosis.

From the viewpoint of the diabetes, th establishment of the symmetrical pneum thorax does not seem to have added elemen of gaseous acidosis, to the acid intoxicatio arising from the diabetes. On the contrar the increased acidosis connected with th installation of the tuberculosis was rath alleviated since the installation of the pneum thorax. The quantity of insulin necessar however, to enable the patient to tolerate

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Think of therapy in terms of the patient

WHEN we treat such conditions as general debility, lack of strength and convalescence we must think of the patient rather than of disease---because the patient has no disease. Our problem is to increase the functional activity and vitality of the patient's tissues and enable the organism to develop more energy.

The new endocrine tonic

INCRETONE

makes it possible to raise the level of metabolic activity and to increase the patient's strength by increasing his energy production.

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restricted carbohydrate diet remains extremely high.

From the viewpoint of their general health, the effect of collapsotherapy is shown in arrest of the fall in weight in one of the patients and gain of 5 kg. in the other.

From the viewpoint of the tuberculosis the expectoration has ceased and fever has fallen.

Moreover, it must be remarked that no signs of cardiac failure have been noted in this patient outside of a transient tachycardia with very transient cyanosis in one of them at the time of the installation of the pneumothorax.

In the discussion, *M. Courcoux* stresses the good influence of pneumothorax on the tuberculosis and diabetes: even without insulin, diabetes may be seen to improve after a pneumothorax has been established if the diet is suitable. Inversely, if the diet is poorly followed, diabetes increases and the tuberculosis is observed to rapidly become aggravated.

M. Rist remarks that these two cases come to the support of the successes which may be obtained with bilateral pneumothorax. The intervention is serious but the fatal prognosis of tuberculosis associated with diabetes should not be forgotten. It is modified since the patients may be treated with insulin and pneumothorax.

M. Carnot has observed a case of diabetes associated with bilateral tuberculosis which occurred despite insulin treatment, where the results of pneumothorax were deplorable.

Spleen and Rickets. — A. Rémond, L. C. Soula and G. Cauquil. (*Bull. Acad. Méd.*, **100** : 825, 1928.)

Rickets does not always have to arise through lack of sterins, but can also be caused through an endocrine insufficiency of their elaboration. This elaboration is normally undertaken by the spleen and reticulo-endothelial system. In rickets this system is insufficient and can be made normal again through treatment with ultraviolet light and organotherapy by means of sterins.

Concerning the Female Sex Hormone. — Laqueur. (*Münch. med. Wochenschr.*, **76** : 177, 1929.)

The female sex hormone can be used in female, especially climacteric, obesity, for its therapeutic effect owing to its action on metabolism. The use of the ovarian hormone in prostate hypertrophy is rejected; on the

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other hand, its administration for the purpose of transient sterility is held disputable. With respect to the antimasculine influence it is stressed that this extends only to the testis. There can be no doubt of the specificity of the female sex hormone in regard to the action on definite systems only, as well as with regard to extraction from definite tissues. With regard to the storage of the female sex hormone, new, partly unexpected experiences are reported which render more difficult the experiment concerning the balance of the hormone, but on the other hand, open therapeutic perspectives.

Recent Investigations concerning Experimental Hermaphroditism and concerning the Antagonism of the Sex Glands. — A. Lipschütz. (*Pflügers Arch. ges. Physiol.*, **221** : 439, 1929.)

Ovary was implanted intrarenally into male guinea pigs with both testes intact. In 3 of 14 experiments the female hormonal effect occurred in the mammary apparatus in the sense of hyperfeminization; in 2 cases secretion of milk and colostrum was also present. The results contrast with all experiments up to the present and may not be attributed to technico-operative factors. The male sex characteristics remain normal in contrast to endocrine active ovaries. All experiments on the capability for reproduction of hermaphroditic males result positively. E. T. Engle (*Proc. Soc. Exp. Biol. and Med.*, **25** : 715, 1928) reports concerning experiments in which he was able to promote the occurrence of female hormonal effects in rats with intratesticular ovarian transplantation by administration of the hormone of the anterior pituitary.

The Reactions of the Organism in the Eczemas. Sensitization Syndrome. — H. Jausion and P. Cot. (*Paris méd.*, **19** : 67, 1929.)

The functional involvement of the endocrine glands in the symptom picture of eczema has been repeatedly demonstrated yet no general rule could be established in these individual findings. H. Vincent assumed a dysfunction of the thyroid as cause of the Malpighi spongiosa; many authors were able to observe a relationship between the onset of eczematous symptoms and the function of the ovary. J. Meyer and Gallerand on the contrary obtained undoubted results through the injection of testis extract in women wi out wishing to assume for this reason a cau relationship with respect to the etiology the disease and the result. The comm embryonal origin of the vegetative and en crine system explains their synergism. It been established that the suprarenals regul the sympathetic tonus and maintain it. W the hormone of the suprarenal effects may attained by the therapist only in very limit degree through adrenalin; this characteri the circle of action of the thyroid hormo also. Garrelon, Santenoise and Legra demonstrated the double function of insul which on the one hand regulates the nature pancreas secretion and on the other, throu maintenance of the vagal tonus, acts on vagotonizing hormone whose secretion activates. In this way, an explanation for t fluctuations of glycemia in sensitized in viduals would also be given. All these fin ings and considerations demonstrate t significance of the endocrino-vegetative s tem.

Edema and Edema Formation. — Jervell. (*Tidsskr. norske Laegeforening*, 4 73, 1929.)

Pernicious anemia is one of the disea in which a tendency to edema exists. Th edemas resemble the nephrotic to a cert degree in their localization. The finding characteristic that these edemas arise in periods of exacerbation of the disease a disappear under liver treatment with rem sion. As cause of the readiness for edema diabetic patients a certain undernutrit must be assumed as etiological factor. Es cially in patients who receive sodium bic bonate, this tendency to formation of ede is to be observed. This question receive special interest at the present time thro the edema frequently appearing during insu treatment. Insulin edemas are most f quently observed in patients who have p viously been in precomatose or comat state. The size of the dose of insulin adm istered as well as the water and salt cont of the diet seem to play a rôle in this. Pet and Odin regard the alkalosis called forth insulin as the most important cause of wa retention. O. Klein assumes changes of bl viscosity through the action of insulin; V mer and Serebriski refer to the antagoni relation between pituitrin and insulin; ot authors bring into consideration the action

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insulin in influencing the amounts of globulin and fibrin in the plasma. The author believes that the formation of edema which is observed during insulin treatment, is to be attributed to changes of the colloid-osmotic pressure of the blood. The possibility is also to be drawn into consideration that the permeability of the capillary is changed in diabetics.

Concerning Female Sex Hormone. — M. Kochmann. (*Würzburger Abhandl. Gesamtgeb. Med.*, 5 : 173, 1928.)

De Veer has obtained from whole ovary as well as from corpus luteum with the aid of organic solvents an extract which influences the metabolism of female animals in a particular manner. In acute experiments of several hours, following injection of this extract, the oxygen consumption rises, whereas the CO_2 excretion increases in the same measure. The respiratory quotient is markedly lowered. Male, sexually mature animals do not show this influence, in contrast to young, sexually immature and castrated animals. Kochmann and Wagner believe from their similar results that they have a new hormonal substance specific for female animals, which they call Oobolin. It is not identical with the menstruation hormone.

Nuernberger used Oobolin in a small number of cases and observed two to three strikingly favorable results in addition to failures or doubtful results. Whether other hormones are also present in Oobolin or whether the estrus hormone also present in Oobolin comes into action the author is unable to say. According to the experience of Hartwich, Kochmann believes that Oobolin might also be indicated in adiposity of ovarian origin.

Organotherapeutic Treatment of the Symptoms of Obesity, Sterility and Migraine in Ovarian Insufficiency. — A. Ulrich-Lévy. (*Progrès méd.*, No. 9 : 380, Mar. 2, 1929.)

Independent of the genital and menstrual disorders which are proper to it, ovarian insufficiency includes a very frequent symptomatic triad: obesity, periodic headaches and sterility. The treatment capable of influencing these three cardinal symptoms effectively may be considered as acting energetically on the ovary itself. Such a treatment should evidently attempt to be pathogenic and should take into consideration the cause of the insufficiency. The classical emmenagogues are of but little assistance. Organotherapeutic treatment is much more logical and causal.

With ovarian extracts and especially with dissociated ovarian therapy (corpus luteum and ovary without corpus luteum), success is frequently obtained. The author has frequently noted the cure of simple ovarian insufficiency particularly in young girls by this method.

In the presence of an adiposogenital syndrome, however, when the obesity occupies a preponderant place, the author prefers the use of spermatogenetic organotherapy. The results which spermatogenetic therapy has given, administered, according to the case, either in injections or orally, are illustrated by six cases reported.

While the author considers that there is indication for ovarian organotherapy in the presence of a hypo-ovarian syndrome, she believes that in certain cases it is preferable to give spermatogenetic organotherapy if obesity, sympathetic disorders with or without psychic disturbances and sterility predominate.

It is of course understood that such a treatment does not exclude any of the adjuvant medications, physical, hydrotherapeutic, gymnastic, etc. Thus, in certain cases thyroid or euthyroid serum has been added to the spermatogenetic extract in order to obtain the maximum therapeutic effect. Thyroid extract and spermatogenetic extract were never used simultaneously, however, as their similarity of action is great enough to contraindicate their use at the same time.

Clinical Contribution to the Question of the Atrophoderma. — O. Blatt. (*Dermatol. Wochenschr.*, 88 : 190, 1929.)

The assumption of the endocrino-sympathetic genesis of this skin process seems to have taken firm ground. The author assumes the common pathogenic factor for this group of skin disorders in the endocrine system. On the basis of clinical observations, acute and chronic infections are regarded as exciting causes (syphilis). Among 38 cases the author found hypofunction of the pituitary in 15 cases, hypofunction of the ovary in 13 cases, hypofunction of the thyroid in 5 cases, hypofunction of the suprarenals in 3 cases, hyperfunction of the suprarenals in 3 cases, hyperfunction of the thyroid in 6 cases, normal function of the thyroid in 5 cases, normal

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function of the ovary in 3 cases, normal function of the suprarenals in 10 cases, normal function of the pituitary in 1 case.

On the Subject of Dermatofibrosis Lenticularis Disseminata. — A. and L. Pokorny. (*Dermatol. Wochenschr.*, 88 : 157, 1929.)

The authors stress the circumstance that the hitherto known four cases concerned women only and that the three cases of personal observation showed internal secretory disorders and relations could be discerned between dermatofibrosis lenticularis disseminata and the ovarian function. In the one woman the dermatosis appeared with the beginning of the menopause; in the younger daughter of this woman the relation of disturbed ovarian activity was still more definite; in the third patient, the older daughter, a polyglandular disorder seemed to be present. In this patient there also exists a certain adiposity which together with the delayed growth in length may be attributed to the small thyroid.

The Action of Posterior Pituitary Preparations on the Intestine

(*Continued from page 329*)

"5. Papaverine antagonizes the morphine action in both types of segments."

There would seem to be no doubt that solutions of post pituitary contain a substance or substances that exert a specific action on the smooth unstriped muscle of the intestine. Histamin and cholin are apparently excluded. The effect is dependent upon the concentration and existing tonus. Both the pressor and oxytocic fractions of pituitary solution give this effect. Clinically it appears to be of value, injected hypodermically, in intestinal paralysis.

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Embolism and Cardiac Syncope T Days after a Laparotomy; Intracard Injection of Adrenalin. Recovery. Lutaud. (*Presse méd.*, 37 : 7, 1929.)

Ten days after an appendectomy and h teropexy a patient suffered from a severe lapse following embolism. The author injec 2 cc. of a solution of adrenalin (1:1000) the heart after the patient's heart had b stilled for somewhat less than 10 minu The woman was not merely momentaneou resuscitated but complete recovery effected.

Lesions Found at Autopsy on a Subj Affected by Adiposogenital Syndrome. Babonneix and Lhermitte. (*Presse méd.*, 3 408, Mar. 27, 1929.)

The patient had suffered from hydrocep lus with hydromyelia and an adiposogen syndrome with polyuria. At autopsy, in ad tion to the hydromyelia, they found a v marked hydrocephalus with atrophy of tuber; they established a relation of ca and effect between these lesions and the s drome.

Tuberculous Ovarian Semi-Sclerosis New Endocrine Syndrome. Its Tre ment. — M. Laemmer. (*Presse méd.*, 37 1929.)

The symptoms of the disease form descri are: dysmenorrhea or amenorrhea, toxic in weight; similar to the forms in hypofu tion of the thyroid where the thyroid, h ever, plays no rôle; traces of signs of a tu culous disease, decalcification and dep phatization (urine analysis); change in b pressure; small, hard ovaries.

Thyroid therapy is quite ineffective. Tr ment with corpus luteum or ovarian ther alone is without result. The following is much more necessary: injections of fol lin every second day, diathermia, diet antituberculous treatment, phosphate, cium.

Inquiry concerning the Cause Treatment of Chronic Joint Disea Introductory Paper. — A. Laqueur. (J *Klin.*, **25** : 137, 1929.)

Among other questions, Laqueur asked what part falls to hormonal causes in chr joint diseases, according to the experie of his colleagues present at the meeting?

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s in recognition of this cause, is the per-entage portion of primary chronic joint heumatism (polyarthritis chronica progres-iva) in the female sex to be supposed to be onsiderably greater than the percentage ortion of infectious arthritis and of genuine rthritis deformans? (3) What therapeutic onsequences does the meeting draw from hese experiences?

H. Schlesinger, p. 138: Hormonal factors ight play only a modest rôle in the origin f chronic arthritis, if one disregards Heber-en's nodules. Schlesinger did not observe onvincing results of hormonal therapy.

J. Breemenvan, p. 138: Among the female atients in the polyclinic suffering from ar-ritis, a great number of the diseases are in l probability to be related to hormonal isturbances. The author believes that ormonal therapy is used with success in arious cases. Thyroidin is especially effec-ve in these cases. Other preparations like ormotone, etc., have occasionally given vorable results.

S. Morawitz, p. 139: Hormonal factors at ast play a decidedly significant rôle as upporting factor in the form of polyarthritis hronica rheumatica which appears in women r the first time in the climacteric or in-reases at this time. Whether such hormonal isorders are able to cause polyarthritis hronica by themselves alone, Morawitz is nable to decide. Hormonal therapy was ever successful in the cases of the author.

P. Köhler, p. 140: Hormonal influences are course of great significance; the ovaries specially play a great rôle in the disease picture of so-called primary chronic joint heumatism; still Köhler does not believe hat there is an independent disease, which is nly conditioned through ovarian glands. he hormones act through the influencing of ineral metabolism, of the autonomic nervous ystem, of the alteration of metabolism of the issues so that the ground is prepared for rthrotropic damage. A hormonal therapy s important as adjuvant and direct influence n the supporting tissue or indirect, for xample, in thyrogenous obesity. The author as not observed a cure of primary, chronic oint rheumatism; on the other hand, admin-stration of hormonal preparations seems to ave a favorable action on the course.

S. Krebs, p. 140: It should be unques-ionable that hormonal causes play an tiological rôle in chronic arthritis, especially in women. Hormonal therapy has brought to light very few uniform results in chronic arthritis of presumably endocrine origin.

Concerning the Influence of Insulin on the Liver. — E. Forsgren. (*Acta med. scand.*, **70** : 139, 1929.)

From the author's experiments it may be seen: that insulin exerts no noticeable action on the glycogen content of the liver and does not affect the rhythmic activity of the liver.

The susceptibility for insulin seems to vary with the rhythmic activity of the liver and to be greatest in the secretory phase when the glycogen content is low.

Practical Therapeutics

(*Continued from page 342*)

ism, such a delicate and nicely balanced mechanism as the central nervous system can not help but be involved. Whether this is what actually does take place, or whether the endocrine dystrophy and the changes in the central nervous system are, alike, the result of some more obscure etiology, possibly of a genetic nature, is yet to be proved. That certain parallels of this character do occur is evident, and there is ample experimental evidence to warrant the belief that changes in the glands alone are adequate to bring them about. The studies of Lipschütz, Moore, Myers, Sand and others upon the male sex-glands following castration and vasectomy prove beyond question the power which these glands, at least, have in influencing psychic development and change. Other equally convincing evidence has been submitted by Cushing, Dercum, Kanavel, Goetsch and others as regards the pituitary, while the psychic relationship of thyroid and pancreas has become well known.

While it is quite true that our knowledge of symptom-complexes is not yet adequate to enable us to definitely fix upon the exact gland or glands involved in many cases, yet it is equally true that while a single gland may be primarily involved in many instances, these manifestations are invariably to be attributed to a derangement in varying degree and proportion, of the whole endocrine system.

Affections of the female sex glands unquestionably have extremely far-reaching and important psychic effects. The high rate of mental disturbances coincident with the onset

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of puberty and with the climacteric is in itself evidence of this, as are the disturbances so often found following castration in the female. The exact relationship existing between the ovaries and mental deficiencies is not clear.

In a summary Downs concludes his paper as follows:

A majority of the endocrine dystrophies present marked and definite psychic symptoms peculiar to their class. It seems probable that both somatic and psychic symptom-complexes are the result of endocrine disturbances, acting upon the entire organism, including also the other glands of internal secretion. It is probable that still deeper than these hormone effects are other more obscure causative factors, which, through the glands of internal secretion, affect the entire organism. It is obvious that the way in which experimentally produced endocrine variations affect the organism is a close parallel to many definitely hereditary aberrations. It seems, then, plausible to believe that heredity may in great part function through the medium of the endocrine system, to produce definite symptom-complexes involving both physical and psychic changes of definite and characteristic types.

Chronic Mental Disease Associated with Ovarian Dysfunction. — Alfred Danby and Kathleen Sykes. (*Lancet*, **216** : 129, Jan. 19, 1929.)

Within recent years a considerable amount of attention has been directed to the organic factor in the etiology of mental disease. In this connection a case is reported the outstanding features of which were the remarkable exacerbations of mental symptoms at a particular phase of the menstrual cycle, and their complete remission after resection of the diseased part of the ovaries.

The irregularity of the menstrual process in interval, duration, and amount was a clear manifestation of disordered ovarian function; the pathological findings were in accord with this.

In view of the present work on estrin, and the apparent physiological antagonism between the estrus-producing hormone and that of the corpus luteum, it seems reasonable to infer that the morbid condition of the ovaries had interfered with the normal correlation of their cyclic functions. Presumably this derangement had thrown out of gear the endocrine balance which, in this instance, had caused a psycho-pathological reaction.

Achondroplasia and Pure Dwarfism Patel and Carcassonne. (*Presse méd.*, 394, Mar. 23, 1929.)

The authors report the case of two dw whom they had occasion to treat for sur affections. One is a subject of 1 m. 37, senting the deformities characteristic of ac droplasia of the rhizomelic type of Pi Marie, as shown by measurements and general appearance of the patient with powerful musculature on the bones of shortened members, his large head and adult's body. Radiography reveals the c sical deformities: The sphenoidal and fro sinuses are enormous; the bones of the m bers have large exostoses. Mentality normal.

Contrasting with the first patient, second is a dwarf of very different type. man of 1 m. 42, the bones of whose memb body and head are small and feeble. It question of purely congenital dwarfism in patient; there is no infectious history, cardiac lesion suggesting dwarfism of infa type (Lorain's type). The thyroid bod normal and the appearance of a minia man is entirely different from the Briss type of dwarf or the myxedematous.

Functional Hemorrhages in Gy cology. — M. Henkel. (*Med. Klin.*, 60, 1929.)

Calcium enrichment of the blood, adm tration of iron and nourishing food are important in the therapy of functi gynecologic hemorrhages. That org therapy plays a large rôle is evident. It however, be made clear that several i tions of a properly chosen hormone can "effect a cure." This will only be the when the endocrine deficiency is not transiently but permanently compens by functional regulation of the organ that can take a long time.

Pituitary — Midbrain System and Metabolism. — W. Raab. (*Wien. Wochenschr.*, **42** : 238, 1929.)

Discussion of the action of pituitrin i metabolism. In the dog, pituitrin caus regular, characteristic effect attained thr no other hormone preparation. To attain pituitrin effect probably very large doses required in the dog with subcutaneous i tion, whereas with injection into the b

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ventricle small portions of it suffice. This behavior shows the correctness of Biedl's assumption that pituitrin acts in the vegetative metabolic center of the midbrain. Following destruction of the tuber cinereum the pituitrin effect remains absent, just as following poisoning with drugs which act in the midbrain: pyramidon, antipyrin, etc.

The conclusion is reached that pituitrin furthers the absorption of fat from the blood on the part of the liver by the above described nerve route and the destruction of this amount of fat in the liver. Numerous clinical and anatomical observations have established the appearance of obesity following lesions of the pituitary alone as well as of the vegetative centers alone and of both at the same time.

T. C. Hunt, of course, missed each effect in obese individuals following several injections of pituitrin (1 cc. daily for 6 to 13 days) in fact small increases in weight even occurred. Nevertheless, the fact of a specific influence of pituitrin on fat metabolism is established on the basis of extensive uniformly positive experimental series.

Concerning the Action of Very Small Doses of Thyroxin on Gas Exchange of Invertebrates. — Romeis and Wüst. (*Naturwissenschaften*, **17** : 104, 1929.)

In investigations concerning the action of mammal hormones on invertebrates, the influence of thyroxin on oxygen consumption of butterfly chrysalis was also tested and an average rise of oxygen consumption of about 30 to 50 per cent was found.

New Methods of Treatment of Exophthalmic Goiter. — B. Aschner. (*Hippokrates*, **1** : 366, 1929.)

Failure is frequent in the treatment of many cases of exophthalmic goiter. Iodin, ovarian tablets and antithyroidin are given and a sensitive stomach is overloaded (which contributes very much to the aggravation of the total symptoms).

The further important factor in the constitutional treatment of exophthalmic goiter is the behavior of the menstrual function. In too weak or infrequent menstruation, ovarian preparations in the form of tablets or injections may be given. Several cases of improvement have actually been observed following ovarian therapy. It must, however, be recalled that ovarian tablets frequently irritate a sensitive stomach very much and may make an existing dyspepsia worse. Ovarian injections bring substances alien to the blood into the circulation and in this way increase the existing autointoxication. The author accordingly prefers emmenagogues.

The skill of the physician consists not merely in using as purely mechanical measure in each patient a few specific remedies such as Basedow-antithyroidin, but in giving each individual case individual attention, as do the homeopaths in their field.

Indications for a Conservative Therapy of Glaucoma. — R. Thiel. (*Therap. Gegenw.*, **70** : 71, 1929.)

Very narrow limits are drawn for the therapeutic use of adrenalin in this complaint. As contraindication are above all to be considered: diabetes mellitus, exophthalmic goiter, severe degenerative changes of the heart and blood vessels. The point of attack of adrenalin in the eye appears to lie exclusively in the vessels according to clinical experiences made thus far. If these are damaged to such an extent that the expansion of the wall as well as the permeability are irreparably disturbed, adrenalin is no longer active. Moreover, a maximum midriasis is occasioned by adrenalin before the desired contraction of the intraocular vessels has appeared in the depths; this midriasis, however, signifies an essential danger for the eye. Adrenalin treatment is most active in acute iritis with rise of pressure and can also be of value in glaucoma simplex. The use of adrenalin is not to be recommended in absolute or hemorrhagic glaucoma.

The Cachexia of Growth, Pluriglandular Syndrome with Pancreatic Participation. Favorable Action of Insulin. — E. May and F. Layani. (*Bull. et mém. Soc. méd. Hôp. Paris*, **45** : 302, Mar. 4, 1929.)

A young girl of 16 years shortly after the establishment of menstruation presented an increase of growth, accompanied by various disturbances, vasomotor manifestations, then a disappearance of menstruation and finally a considerable loss of weight. At the same time there was a slowing up of nutrition as shown by the low basal metabolism.

These disorders are of interest in their grouping and their intensity. They furnish an exaggerated picture of the findings observed in young people of both sexes at the time when they are growing and when sexual

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function is established. In general, however, all these disturbances attain only moderate intensity. In the present case the intensity of the manifestations of growth was sufficient to cause hospitalization. The emaciation especially was actually impressive and justified the name of cachexia of growth. The appearance of this disorder at the time of puberty tended to incriminate endocrine disturbance and the pronounced emaciation suggested the idea of pituitary cachexia. The ovary also played a rôle in this case as shown by the arrest of menstruation and the exaggeration of the cyanosis of the extremities. Moreover, the great fall of basal metabolism hardly ever exists at such a low state without a weakening of the thyroid function. Finally, the action of insulin on emaciation suggests a pancreatic deficiency. The cachexia of growth accordingly appears to be essentially a pluriglandular syndrome. At the time of life when the child is transformed into the adult it requires a common effort of all the endocrine glands. In certain subjects probably presenting a congenital or acquired glandular debility, the endocrine apparatus is unable to furnish this effort and gives signs of failure. In this pluriglandular syndrome a part should be given to insufficiency of the endocrine pancreas. In this patient the pancreatic deficiency was manifested by a considerable emaciation but without diabetes.

Treatment gave very interesting results which showed to what extent the various endocrine glands in the true pluriglandular syndromes may remain independent of one another despite the common signs of deficiency. The action of insulin was striking on the emaciation but on this symptom alone. With 10 units of insulin daily for 6 weeks, the patient regained 15 kilograms between the beginning of June and the middle of September and this gain in weight continued more slowly after cessation of the insulin therapy. On the other hand, menstruation did not return and basal metabolism remained as low as at the beginning of the treatment. Only after another specific therapeutic treatment, thyroid and ovarian, did the metabolism again become normal and was menstruation reestablished. Thus, the pluriglandular deficiency reacted only to its particular stimulus and the authors believe it well worth while to direct attention to this independence of the various elements of the pluriglandular syndrome. They were especially surprised to observe great emaciation coinciding with fall of basal metabolism. It is difficult t understand how an improvement in assimila tion as shown by a gain of 18 kgm. should no be accompanied by a parallel modificatio of the basal metabolism. It must then b admitted that the relations which unit basal metabolism and the activity of th nutrition are more complex than one woul think at first glance.

The authors' observation also shows wha favorable results may be obtained in state of difficult growth and denutrition of puberty

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William Stokes

(*Continued from page 345*)

were nights of entertainment with music i which Stokes himself was well informed, a well as an accomplished player; there wer also discussions in art with Petrie, and timel topics of the world in general. (It was at on of these gatherings that Carlyle met Stokes. Stokes was no politician; he did not care t mix in the affairs of "Young Ireland," yet h did not cease to be a patriot. He states, o the contrary, "To me the real patriot is h who, in a life of labour and of trial, wit integrity, practical wisdom, and far-seein intelligence, labours onward to no other en but that his country shall rise, and with th honourable and justifiable ambition that, lo ing her, he may rise with her also."

For all his energetic nature and brilliar career Stokes remained a benevolent, cha itable person, always seeking thoughtfull and wisely to alleviate the pain of the sick an bereaved, not only in his work but also in h home. Sir Henry Acland says of him that h combined "real delight in all intellectu development with the deepest sympathy fo suffering." He was universally acclaimed b men of his profession as well as by those who he treated in the clinics, by his associates an by his well-loved family. The closing years o his life were saddened by the disintegratio of his family circle through sickness and death After the loss of his wife his interest in livin seemed to wane, his energy and vitalit decreased so that he was incapable of pursu ing the industrious method of work he ha enjoyed previously. One day, in steppin from a carriage Stokes suffered a fall whic ultimately caused his death (January 6, 187 from a paralytic seizure.

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Investigations concerning Elective Nutrition and Growth. — H. Reiter. (*Med. Klin.*, **25** : 268, 1929.)

In the investigations undertaken it was a question of clearing up metabolic processes, which are closely connected with a feeding of elective food complexes; in particular the influence of administration of certain food mixture on growth should be more closely investigated. As food substances added to the diet, liver substance and beef testis substance were chosen. The latter was at the same time observed for the presence of a sex specific action through enteral administration. Investigation was also made whether this addition to the diet succeeds in again completely removing the disease picture induced in animals by the Stepp diet.

In the investigations undertaken it could be shown that liver substance, relatively sparing, freed from moisture and not to be considered as denatured, as well as testis substance treated in the same way, not only supplies the deficiency of the Stepp diet but even as a rule very rapidly and completely alleviates the injurious effect of the Stepp diet. The intensity of growth is extraordinarily strongly favored by administration of non-denatured substances, and leads to considerable weight values in male animals, under the use of testis substance. The intensity of growth corresponds to the value of the hemoglobin content and the erythrocyte count.

Concerning the Delay in Consolidation of Fractures Due to Syphilis (Unknown). —L. Bory. (*Progrès méd.*, **56** : 343, 1929.)

In a 25 year old patient a fracture of the leg failed to consolidate within 9 months. When syphilis was noted on the basis of a positive Wassermann reaction, a specific treatment was first given and later a general treatment with organotherapy. The patient received a calcium preparation in which a thymus powder (0.20 gm.) and a parathyroid powder (0.30 gm.) were combined. After 7 weeks, the complete consolidation was demonstrable clinically as well as radiologically.

Diabetes and Exophthalmic Goiter Associated. — M. Labbé and Gilbert-Dreyfus. (*Paris méd.*, **19** : 429, May 4, 1929.)

Diabetes mellitus is so frequently found associated with exophthalmic goiter in the clinic that we can not speak of a simple coincidence but must admit an actual morbid relation. Moreover, the constant disorder of glycoregulation revealed by the test of hyperglycemia in exophthalmic goiter shows that thyroid hyperactivity exercises an influence on the metabolism of sugars. The frequency of this association is not very great. The goiter is most frequently the first to appear and diabetes takes second place. Sometimes, however, it is the diabetes which occurs first. According to statistics, of Joslin and Lahey and Wilder, it is the toxic adenomatous or secondarily basedowified goiter which is most often accompanied by diabetes. Primary exophthalmic goiter is a little less frequently responsible. The observations resemble each other sufficiently to characterize a special clinical type. When the pathological picture is complete, it is that of an intense exophthalmic goiter in which the basal metabolism reaches a high level, higher on the average than that of isolated exophthalmic goiters, according to Joslin.

The diabetes may show all the degrees of severity: at times benign, representing a thyroid glycosuria rather than a true diabetes, at times diabetes without a nitrogenous denutrition, of moderate intensity, at times severe diabetes with nitrogen denutrition and acidosis.

Death is most often due to coma. It is generally an ordinary acidotic coma, at times it is a state of cardiac collapse associated with acidosis. This was the case in the observation reported. In the majority of cases the diabetes and the exophthalmic goiter evolve together, undergoing simultaneous exacerbations. This is not observed in all cases.

The frequency of association of diabetes with exophthalmic goiter, the evolution by simultaneous exacerbations of the two diseases suggested to M. Labbé that there might be a thyroid diabetes under the jurisdiction of a special pathogenic mechanism distinct from that of the usual pancreatic type of diabetes. In thyroid diabetes disturbances of glycoregulation would be due to hyperthyroidism whereas in pancreatic diabetes it is due to insufficiency of the insulin secretion. We know that the glycoregulative function is complex and that various organs participate in it. Among these the pancreas and the thyroid play an antagonistic rôle. Numerous animal experiments and clinical observations on exophthalmic goiter patients unite in bringing to light the rôle of hyperthyroidism

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in the pathogenesis of glycoregulative disorder. These experiments tend to show that hyperthyroidism may create a true diabetes in which the liver has become incapable of retaining glycogen just as in ordinary diabetes where insufficiency of insulin has likewise abolished the glycogenic function. This thyroid diabetes must follow the same evolution as exophthalmic goiter.

All the authors admit that active treatment of the exophthalmic goiter with iodin, x-rays, thyroidectomy simultaneously exerts a favorable action on the associated diabetes. This action is however not always easy to show. The authors report a case in point in which iodin on two occasions had a very definite moderating effect on the exophthalmic goiter; diet and insulin acted very effectively on the diabetes; insulin had no action whatever on the goiter; iodin (after having improved the goiter) did not seem to simultaneously ameliorate the diabetes at the beginning but contributed to its improvement in a later phase.

The demonstration of the improvement of diabetes by the intervention of improvement of exophthalmic goiter by iodin treatment is not as definite as could be expected and the experiment should be undertaken again. Nevertheless it seems that the diabetes while reacting distinctly to diet and insulin was also influenced by antithyroid medication and behaved like a thyroid diabetes. In the presence of these facts we arrive at a less simple conception of diabetes in exophthalmic goiter patients than before.

Basedowian diabetes is fundamentally an ordinary diabetes due to insufficiency of the internal secretion of the pancreas like all diabetes; it reacts to diet and insulin like all the diabetes. Yet it is distinct from ordinary pancreatic diabetes because it evolves simultaneously with exophthalmic goiter and because it is at times less definitely sensitive to the action of diet and insulin. In reality its pathogenesis is complex. The disorders of glycogenic function result here not only from insulin insufficiency but also from excess of secretion of thyroxin. Hyperthyroidism which would not itself be capable of creating a severe diabetes may very easily aggravate a moderate diabetes associated with intense pancreatic insufficiency. It lowers the capacity for utilization of carbohydrate, it produces nitrogen denutrition, it excites acidosis; finally, it may render the subject relatively less sensitive to the action of diet and insulin.

Thus, pancreatic hypo-insulinism and th roid hypersecretion add their effects to pr duce a diabetes of serious type. At the san time the treatment of this diabetes deman the cure of the exophthalmic goiter at th same time as diet and insulin therapy. Th cure of the exophthalmic goiter improved th diabetes but did not suppress it.

It remains to learn why diabetes is mo frequent in exophthalmic goiter patients tha in ordinary subjects. Is it because the hype thyroidism reveals a moderate insulin diabet which without it would have remained latent Is it not rather because of a coincidenc rather frequent in affections of the variou endocrine glands, an endocrine synergism In any case, these endocrine interrelation were interesting to study to understand th pathogenesis and clinical evolution of th diabetes associated with exophthalmic goit and to arrive at a curative therapeut method.

Experimental Researches on the Cor pus Luteum. — L. Brouha and H. Simo net. (*Presse méd.*, **37** : 591, May 4, 1929.)

Injected into normal female rats, extrac of corpus luteum permit the suppression of th estrous cycles if the dose is sufficient. Th genital tract then assumes an aspect analogou to that found in the castrated animal. Wit smaller doses there is created a state reca ing pseudo pregnancy with characteristi estrus but with development of the uteru With very small doses there is simply pr longation of the interestral periods.

In the immature animal the extracts reta the appearance of the first estrus. In the ca trated animal they do not provoke any dev opment either of the uterus or of the mam mary gland. The extracts act on the estr phenomena probably by suppressing the pr duction of folliculin and not its action, for, we inject folliculin and extract of corp luteum simultaneously, the latter does n prevent the effects of folliculin from showi themselves.

Anterior Pituitary Hormone and Mal Genital Tract. — L. Brouha and H. Sim onnet. (*Presse méd.*, **37** : 591, May 4, 1929

Daily intramuscular implantation of fra ments of anterior lobe of pituitary shows th this gland exerts a marked stimulating acti on the male genital tract (rats, mice). Th action of anterior pituitary extracts vari

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with the method of preparation and sometimes with the dose used. In utilizing the active principle contained in the urine of a woman at the beginning of pregnancy, there is regularly observed an enormous development of the genital tract in the immature animal and in the adult.

With anterior pituitary extracts prepared by alkalin route, a certain development is obtained with small doses; on the contrary, with large doses an arrest or regression. It is not yet known whether these effects are due to two antagonistic substances or to a single substance acting differently according to dose injected.

Concerning the Action of Kidney Extracts. — E. Freund. (*Wien. klin. Wochenschr.*, **42** : 696, 1929.)

The study of the chemical function of most organs has remained a very limited one. The author has already drawn attention to the fact that it might be the task of organotherapy to extract the active substances in all organs and above all in the kidneys and to test them for their therapeutic action.

Concerning the Weakening of the Toxicity of Adrenalin by Some Organic Substances. — G. Boivin. (*Paris méd.*, **19** : 520, 1929.)

The author studied the mechanism of the lowering of the toxicity of adrenalin through aqueous alcoholic extracts of organs. He criticizes the use of a pancreas extract for this type of investigation, since his own studies showed him that the majority of the other organs possesses the same action, and stronger than pancreas extract, if they are injected into rabbits at the same time as the adrenalin. As regards the protective action of a pancreas extract injection in acute pulmonary edema, this is not constant. From the therapeutic standpoint this does not appear to have any interest.

A Case of Exophthalmic Goiter Refractory to Insulin. — W. Kreiner. (*Deut. Zeitschr. Chir.*, **216** : 285, 1929.)

Report concerning a patient with exophthalmic goiter which is noteworthy because of refractory behavior to insulin with simultaneous excretion of sugar. Following removal of the purely parenchymatous goiter, recovery of the patient occurred with no excretion of sugar.

Dependence of Vagus Tonus on Adrenalinemia. — G. Viale. (*Klin. Wochenschr.*, **8** : 73, 1929.)

A number of harmonious experiments have led the author to make the assertion that the tonus of the heart vagus is dependent on the amount of adrenalin circulating in the blood, and that the acceleration of the pulse which is normally to be observed following division of both vagi, is not dependent upon the suppression of an autochthonous tonus of the vagus centers but initially upon an increased secretion of adrenalin, later upon a sensitization of the heart under the influence of the vagi to the adrenalin.

Experiments undertaken by the author led him to the conception that the vagus tonus represents less an autonomic condition of the corresponding centers than the action of adrenalin on these. If adrenalin is deviated, the vagus tonus also comes to nothing. That adrenalin also possesses a vagal action has recently been stated by Smirnow as well.

The vagus tonus which in general is regarded as the expression of the autochthonous activity of the corresponding nerve centers is dependent upon the lasting presence of adrenalin in the circulating blood.

Remarks Concerning Niehans: "Endocrine Glands and the Methods of Rejuvenation." — Enderlen. (*Schweiz. med. Wochenschr.*, **59** : 264, 1929.)

In transplantations of glands executed by him, the author observed necrosis of the transplant in all cases.

Local Anesthetics and Suprarenin. — Eduard Rentz. (*Arch. exp. Path. u. Pharmakol.*, **144** : 310, 1929.)

Tests on the effective capacity of suprarenin in conjunction with members of the cocaine group, gave the following information. The effect of suprarenin, 1:10 millions, is increased by cocaine derivatives. The constricting effect on the blood vessels is not intensified by suprarenin in slight concentration, rather this furthers the vasodilating effect of the cocaine after the initial constriction. With the administration of suprarenin in stronger concentrations, the antagonism of several cocaine derivatives was overcome, partly, and the suprarenin effect, even if decreased, lasted for days. By means of cocaine, novocaine, alypin, and psicaine the effect of suprarenin was inhibited or increased, but not greatly reversed.

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EQUALIZE THE SUPPLY OF INTERNAL SECRETIONS AT THE MENOPAUSE

"Of what does the 'endocrine crisi of the menopause' consist? Or i other words what glandular elemen usually take part in it? I believ these three, the genital, the thyroi and suprarenal are the fundamenta elements entering into the develop ment of the crisis."

(Gregorio Marañón, *The Climacteric,* 192



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Clinical Contributions on Diseases of Metabolism. II. Corpulency and Obesity. — P. F. Richter. (*Deut. med. Wochenschr.*, **55** : 1575, 1929.)

Gland preparations are very important, above all thyroid gland preparations, in the accomplishment of modern therapy of obesity. There are, besides, cases of extensive "corpulency" in which, however, a certain endogenous storage and deficient adaptability of the thyroid gland function and therewith of the oxidation of the over-nutrition, are quite commonly evident.

If the diabetic preparations do not act effectively in these instances, the therapy may be supplemented by thyroid dosage without hesitation, naturally under certain precautions. These are large dosage (0.1 per dose to 0.3 per day) and avoidance of a treatment of long duration (not over 4 weeks), no strict dietary restrictions and finally interception of the thyroid treatment with the occurrence of weakened condition of the heart. One can fare as well as ever with oral administration. Rather rigorous limitations are thus placed on treatment with organ preparations in cases in which previous thyroidized constitutional and endocrine impetus form the chief factor of the existence of the obesity.

Especially in the chief form, "the thyrogenous" obesity, one ought not lose too much time with diabetic preparations, but quickly seize upon the thyroid gland preparations without too strict dietary limitations, which, experimentally, are not very necessary here; but if there is a question of albumin, the effect of thyroid gland on the decomposition of albumin can lead to harmful results.

Success is usually obtained in oral administration of any one of the numerous preparations in the field. The purification of the active principle of the thyroid gland by Kendall (thyroxin) unfortunately has not accomplished the desired effect which one might expect of extract dosage, at a time when one is most inclined to parenteral dosage, for it has the disadvantage of requisite long treatment. Over and against the increased oxidation accomplished with thyroid gland, other organ preparations are valuable. Metabolism is only slightly increased with ovarian preparations. It is not much more increased with pituitary preparations. Of these latter, the secretion of the anterior lobe possesses a slight metabolism-increasing effect which can hardly be considered practical. In most cases the treatment with thyroid gland suffices. The numerous pluriglandular products which contain the hormones of the thyroid gland, ovary and pituitary are only effective in their thyroid gland substance. In the treatment of obesity as such — a favorable effect on many accessory symptoms must not be slighted — the preparations are superfluous if they are not accurate in their thyroid gland content, indeed they are often harmful. In no case must they be prescribed without the control of a physician.

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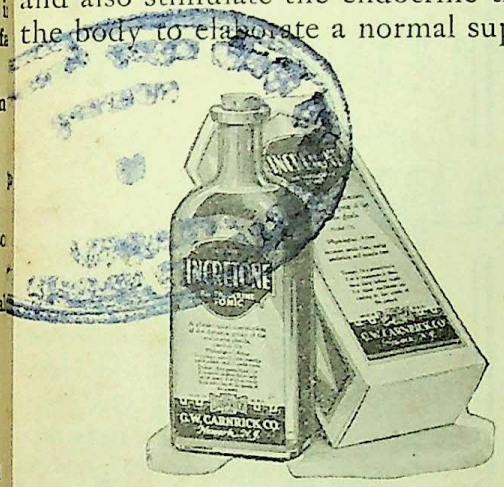
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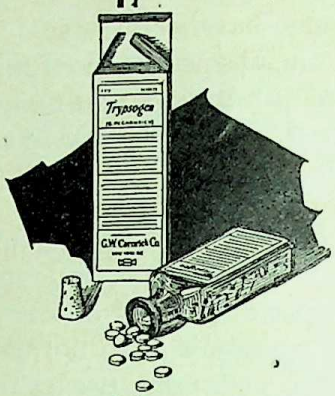
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Exophthalmic Goiter

A DISTINCTION is frequently made between "true" exophthalmic goiter and toxic adenoma. This distinction is here discussed.

(CONTINUED FROM VOL. XIII, NO. 6)

In preceding articles we have reviewed the current views on etiology and pathogenesis. Four major theories of the latter were discussed — thyreogenic (including dysthyroidism), neurogenic, constitutional hyperreactivity and thymic constitution. This article deals with the condition now usually described as toxic adenoma of the thyroid and its relation to exophthalmic goiter. In a recent article[1] Ginsburg reviews the work of the several observers who have described this syndrome and gives the following list of authors and the names under which they describe it.

"Enlargement of the thyroid gland in connection with enlargement or palpitation of the heart — Parry (1825).

"Constitutional iodism — Rilliet (1859).

"Iodine exophthalmic goiter; iodine Graves' disease — Trousseau (1860).

"Formes frustes exophthalmic goiter — Trousseau (1862); Marie (1883).

"Secondary Basedow — Gautier (1893); Buschan (1894).

"Basedowified goiter — Marie (1897); Struma basedowificata — Kocher (1906).

"Goiter heart — Kraus (1898).

"Iodine thyroidism — Breuer (1900).

"Basedowid — Stern (1908-1909).

"Toxic nonexophthalmic goiter — Plummer (1912).

"Toxic adenoma of the thyroid — Plummer (1913).

"Adenoma with hyperthyroidism — Plummer (1916).

"Hyperfunctioning adenomatous goiter — Plummer (1921).

"Iodine hyperthyroidism — Jackson (1924).

"Nodular goiter with hyperthyroidism — Rienhoff (1927)."

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In recent years the name of H. S. Plummer has become more closely associated with the conditions than any other. In numerous publications he has set forth his views, distinguishing toxic adenoma as a condition apart from exophthalmic goiter. "In terms in common use in American literature, the best grasp of the subject can be obtained by classifying goiters as endemic and exophthalmic. The endemic goiters may be divided into the diffuse colloid and the adenomatous; and the adenomatous into those with and those without hyperfunction . . . ."[2].

"ENDEMIC GOITER. — A supply of iodin adequate for the proper functioning of the thyroid, followed by a subnormal delivery of thyroxin to the tissues, produces hypothyroidism; consequent elevation of intensity of thyroid stimulation causes diffuse hypertrophy of the thyroid; the secretory processes are altered; the diffuse hypertrophy disappears; colloid is stored in excess of the normal, and diffuse colloid goiter is the result. In many cases the sustained stimulation of the thyroid, in conjunction with unknown factors, causes the development of new tissue, adenomatous goiter. Relatively late in the life history thyroids containing this tissue in many instances hyperfunction, and the entity hyperfunctioning adenomatous thyroid appears.

"EXOPHTHALMIC GOITER. — Intensive stimulation, of unknown origin, of the entire functionally capable and probably primarily normal thyroid causes diffuse hypertrophy; an abnormal amount of thyroxin and an abnormal thyroid product is delivered; during periods of remission of intensity of stimulation and an adequate iodin supply, the diffuse hypertrophy disappears in some instances and colloid above the normal amount is stored. Under the stimulation, acini which are possibly more or less new, as a rule, develop. In exceptional cases the gland, particularly after a portion has been resected, becomes much larger from the development of new tissue. This should be sharply distinguished from the adenomatous tissue frequently present bef the onset of exophthalmic goiter. In t Mississippi Valley where the incidence of e demic goiter is high, about 30 per cent of t cases of exophthalmic goiter are superimpos on adenomatous goiter."

The subsequent development of this n type of tissue in adenomatous goiter is d scribed by Plummer as indefinite. "Little known regarding the duration of the norm life of the vesicles and the systematic develo ment of new vesicles to replace those e hausted. The interest of the clinician and t pathologist centers largely in the developme of groups of new acini that cannot be co sidered normal. Woefler contributed mu to the subject of adenomas of the thyro and made the observation that they devel from fetal rests. That anyone has actua traced the development of new acini fr embryonal tissue is open to question. T groups of new vesicles may be very circu scribed and few in number, or distribut widely throughout the gland. The tissue m be encapsulated (true adenoma) or none capsulated (adenomatosis). In many ca a sharp distinction between encapsulated a nonencapsulated tissue cannot be made. Th there is some difference in the factors enter into the histogenesis of nonencapsulated a nomatous tissue, widely distributed throu out the thyroid, and circumscribed encap lated adenoma cannot be questioned. Und the terms 'adenomatous tissue' or 'adenom tous goiter' both types are included. In so adenomatous tissue, vesicles in all sta of development may be observed. The lumi of the so-called fetal acini contain no colle and the cells present the general appearan of not having functioned. The fully develop new vesicles show the same histologic e dence of function as the normal vesicles a hence cannot be distinguished individua from the vesicles of the surrounding norm gland tissue. Depending on the relati number of adult vesicles, adenomas are clas fied as fetal or adult. In many adenomas

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high percentage of all the vesicles contain colloid and the new tissue is termed colloid adenoma. An isolated section of such tissue may not be distinguishable from the surrounding normal or colloid-distended thyroid. . . ."

"Two theories prevail regarding hyperfunctioning adenomatous thyroid: first, that the adenomatous tissue elaborates and delivers an excess of thyroxin; and second, that it in some way stimulates the surrounding thyroid tissue to hyperfunction. Although the questions must still be considered open, the evidence accords best with the theory that the adenomatous tissue hyperfunctions. To avoid this question in goiter classification, I have used the term hyperfunctioning adenomatous goiter which, so far as this point is concerned, is noncommittal. Irrespective of the question of which type of tissue furnishes an excess of thyroxin, there is no doubt that the adenomatous tissue actually elaborates thyroxin and stores colloid and iodin. In the following discussion of adenomatous goiter, the facts may be coördinated with either theory; however, I have assumed that the adenomatous tissue hyperfunctions.

"In most cases adenomatous goiter has its inception in colloid goiter. The embryonal cells seem to be stimulated through the same mechanism that forces the gland to maintain a normal level of thyroxin in the tissues. Possibly we should look on adenomatous tissue somewhat as a compensatory attempt. Such a theory does not eliminate the possibility that the formation of the new tissues may in some or all instances be determined by local irritants. Early in its life history adenomatous tissue cannot function. A number of observations suggest that it can elaborate and store colloid long before it can elaborate and store thyroxin. Only rarely are the factors such that the adenomatous tissue will function, at least to the point of causing hyperthyroidism, before the latter half of the third decade of life, although as a rule, it is palpable in the second decade. Only 5 per cent of the hyperfunctioning adenomatous thyroids coming under observation at the Mayo Clinic are in patients under thirty years of age. These constitute about 5 per cent of all adenomatous thyroids resected in patients under the thirtieth year. Sixty per cent of all adenomatous thyroids, resected in patients after the sixtieth year of life, are hyperfunctioning. The average interval between the time the goiter is first noticed and the onset of hyperthyroidism, including only those that hyperfunction before coming under observation, is seventeen and six-tenths years. Although the normal stimulating mechanism seems to be a factor in the inception of adenomatous goiter, once this tissue has started to function it does so erratically without relation to the demands of the organism. This observation is borne out by the fact that the basal metabolism drops to normal, but not below, within eighteen days after resection of the adenomatous tissue and there is no tendency to recurrence of the hyperthyroidism.

"It may readily be conceived that in this postnatally developed tissue the mechanism of coördinating its functional activity with the demands of the body is not fully developed. There is no apparent reason for the onset of hyperthyroidism in the majority of cases. It may be inferred that the adenomatous tissue has an inherent tendency to hyperfunction which is favored by various factors. The increased rate of exhaustion of thyroxin and the resulting elevation in the intensity of stimulation of the thyroid, which we have reason to assume exist in conditions such as essential hypertension, pregnancy and pituitary disease, probably favor the development of adenoma and not infrequently excite adenomatous thyroids to hyperfunction. In these cases the tendency to store colloid is, in general, inverse to the tendency to hyperfunction."

There has been no final acceptance of the duality of these conditions, however. Grouped on either side are equally well known authori-

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ties. Some consider toxic adenoma a distinct entity, others regard it simply as a phase of true exophthalmic goiter. Ginsburg's (*loc. cit.*) conception fairly represents the latter view.

"In recognizing toxic adenoma as a clinical-pathologic concept, I wish to stress strongly that neither clinically nor pathologically do I perceive any fundamental distinction between toxic adenoma and exophthalmic goiter except as the variation of a single disease. Nevertheless, for practical diagnostic and therapeutic reasons, the recognition of this variation is important, for in toxic adenoma the ocular signs are rarely present, the adenoma or adenomas may be small and readily disregarded if stress on this variation in thyrotoxicosis is omitted from the medical literature.

(*Continued on page 36*)

A Contribution to Kottmann's Reaction

(Translated from the article by Dr. Emil Walder, *Mitt. Grenzgeb. Med. u. Chir.*, 1926, 39 : 626, No. 4/5.)

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(Continued from Vol. XIII, No. 6)

In this tenfold stronger concentration of the reagent probably the albuminous substances of the serum, in their function of dispersing agent, result in the ensuing colloidal silver iodide, and the silver is so strong in the background that quite possibly one sees a reaction totally differing from the Kottmann reaction. In so strong a concentration it is possible that most of the silver iodide formed does not remain as a colloidal solution, but instead precipitates out directly.

In addition to the already mentioned difficulties and sources of error of the Kottmann reaction we were led to another point, namely, to the study of the internal mechanism of the reaction by the circumstance mentioned at the beginning that the result of the reaction is in high degree dependent on the succession of addition of the reagents. In this way we hoped to obtain at the same time a clearer insight into the nature of the reaction. In regard to it this also happened to give an experimental proof for the interpretation which Kottmann gives the reaction, by another route. In this respect a colloid chemical work of Lottermoser came to our assistance which states the following:

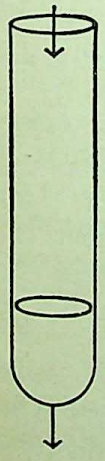
If we add potassium iodide in drops to silver nitrate with shaking, dissolved colloidal silver iodide is formed in which the silver ions present in excess are adsorbed. There accordingly arises a positive charged colloid to which we can give the following formula: $\boxed{AgI.}$ Ag.+. The dissolved colloid state of this combination is related to a positive superfluity of Arg. nitr.; as soon as we have added the equimolecular amount of potassium iodide, everything is precipitated out as silver iodide. If we do the reverse, we add silver nitrate in drops to a solution of potassium iodide with shaking, then dissolved colloidal AgI likewise arises, but this time with adsorbed iodin ions hence a negative charged colloid which may be represented schematically thus: $\boxed{AgI.}$ J.

We utilized these facts in the Kottmann reaction. In the first case there according arises the positive charged AgI with adsorbed silver ions. If we add hydrochloric to this, the Ag ion loosely adsorbed in the A

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is immediately extracted, that is, reduced to metallic silver, which may be recognized by the blackening immediately appearing. The negative charged colloid in which the silver is disguised, that is, is found in chemical combination with the iodin, is only very slowly reduced by hydrochinon. We can, therefore, enlarge our conception somewhat if we consider that during the addition of potassium iodide to silver nitrate there is a point where the colloidal iodide of silver has adsorbed a maximum of silver ions, where accordingly, in other words, there is a maximum of ion colloid in solution as disperse phase. If we add more potassium iodide, then the precipitation of undissolved silver iodide begins, since the iodin ions of the newly added potassium iodide unite with the adsorbed silver ions and the electrical charge which the colloid held in solution accordingly vanishes. The adsorption combination is broken up and the silver iodide is precipitated. These colloid salt solutions are very unstable since it is a question of pure colloid solutions without protective colloid, and it is probable that only the positive or negative charge which these colloids receive through the adsorbed Ag or iodin ions maintains them in colloid state. It seems to us very possible that impure works (sweat colloid, alkalin splitting up of glass) can favor the precipitation of these very unstable formations. Provisionally we believe that we have purely empirically come closest to the optimal point where most Ag ions are adsorbed in the colloid AgI (perhaps this point may be determined mathematically on the basis of Freundlich's absorption law) in such a manner that we add 3 c. c. of a 30 normal potassium iodide solution in drops with shaking to 5 c. c. of a 30 normal Arg. nitr. solution. These amounts correspond approximately to those given by Kottmann. In most cases we have then none at all, in other cases a beginning microscopically visible precipitation in flakes of an undissolved silver iodide. From this mixture we very rapidly pipetted off 0.5 c. c. and added this by mixing to 1 c. c. serum, light with 400 candles for 20 minutes and later add 0.5 of a freshly prepared 0.25 per cent hydrochinon solution, again mix and then read every five minutes for a half hour. We can summarize both mechanisms into one outline:



$\frac{n}{30}$ KI— in drops

$\frac{n}{30}$ $AgNO_3$— in excess

Colloidal $\overline{|AgI.|}$ Ag+
Addition of Hydrochinon

Immediate Reduction
(Immediate Blackening)



$\frac{n}{30}$ $AgNO_3$— in drops

$\frac{n}{30}$ KI— in excess

Colloidal $\overline{|AgI.|}$ I−
Addition of Hydrochinon

Very Slow Reduction
(No Blackening, Only Blue-Gray Coloration)

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In this way we hoped to obtain, therefore, a similar reagent for all sera, if not ideal, at least as constant as possible; we were, however, very conscious that these ionic colloids represent very sensitive, exceedingly unstable formations.

Our procedure is to be differentiated from that of Kottmann in that we add the finished AgI. Ag^+ to the serum, whereas according to Kottmann potassium iodide is first added to the serum, wherein Kottmann to be sure does not make any statement whether the potassium iodide should be mixed with the serum and then first the $AgNO_3$ should be added or whether it should be mixed first after the addition of the Arg. nitr. These things are of very great importance from the colloid chemical viewpoint and in our opinion can be decisive for the result of the reaction; the sequence of the addition of the reagents, of the time in which they are mixed, even the intensity of the mixture, play a great role in such reactions. It would, of course, be ideal to let the AgI. Ag^+ arise directly in the serum adsorbed in the serum colloid, since one would then have a better guarantee for the fact that the dispersion of the colloid silver arising later through the reduction through hydrochinon is actually a measure for the dispersion of the serum. The realization of this requirement is, however, very important since we do not as yet know what occurs when we mix serum with potassium iodide and then by way of supplement add Arg. nitr., what reactions appear between serum and potassium iodide, whether following addition of Arg. nitr., colloid silver iodide actually arises. We prefer, accordingly, to mix the colloid silver iodide in prepared form with the serum. For this procedure it was determinative that we obtain (after thorough experimental testing of each conceivable sequence of the combination of serum and reagent in the above mentioned type) the most constant results in harmony with the clinical history of the cases, in which in the above mentioned way certain colloid silver iodide was added to the serum. S another factor strengthens us in our p cedure: We thought of the possibility t relations might exist between the gold co and the Kottmann method (protective tion) and in the gold count method the col is also mixed with the serum in prepa form (colloid gold). In order that, acco ingly, a reduction in sufficiently mar measure and in conceivable time appe we must allow the above mentioned A Ag^+ to arise; potassium iodide must, the fore, be added in drops to the silver nitr and the latter must be present in exc Now the following objection could be ma since hydrochinon also immediately redu silver nitrate, then in the Kottmann re tion not the AgI. Ag^+ is reduced but the cess $AgNO_3$. We also took this object into account and performed extensive periments of which we mention only following here:

I. Serum 1 c. c. plus $AgNO_3$ (0.5 cent) 0.3 c. c., light and addition of hyd chinon: no reduction.

II. Serum 1 c. c. plus $AgNO_3$ (0.5 cent) 0.3 c. c. plus KI (0.5 per cent) 0 c. c., light and addition of hydrochin reduction.

In experiment No. I, to be sure, more $AgNO_3$ is contained than in No. II. Red tion does not appear in I since $AgNO_3$ co bines with the albumin substances, ph phates and chlorides, etc., of the ser The excess $AgNO_3$ in experiment II is combined with these substances, there it is shown that the $AgNO_3$ is not the s stance reduced.

There still remains to be investiga the dependence of the possibility of reduc hydrochinon from its colloid condition, fr the alkalinity of the medium or of the and OH^- ionic concentration and the fluence of the percentage albumin cont of the sera. The latter could be estima rapidly by the refractometer. Moreov the gold count of the sera must be determin

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parallel with the Kottmann reaction — we have already referred to this point — to see whether relations do not exist between both methods (protective action). Finally, the amount and concentration of reagents used in the reaction appear to be too large.

We now tried to represent the course of the reaction graphically and wished to see whether we could obtain definite curves for exophthalmic goiter on the one hand and for cretins on the other; the course of the reaction is nevertheless too inconstant in the majority of cases; to represent it graphically, accordingly, has above all no signification.

If the reaction were once improved according to the hitherto mentioned viewpoints, it would perhaps be possible to record the course of this graphically and for example to set up definite types of curves, as it were specific curves, for different pathological conditions.

In the investigation we proceeded in the following way:

The blood was drawn by means of a Wassermann needle from the obstructed arm vein in the morning with the patient in fasting condition, and collected in a sterile test tube wrapped in black paper and of ordinary glass; following the removal the test tube was closed with sterile cotton wadding and kept in the dark at room temperature. The goiter venous blood serum was drawn in exactly the same manner when it took place before luxation of the goiter, which was not always possible, to be sure; the luxation took place, however, in so sparing a manner that it could hardly have an essential influence on the result of the reaction through expression of thyroid substances into the circulation. We then allowed the blood to coagulate and in very many cases we had to centrifuge it owing to the insufficient separation of serum there and coagulum (exophthalmic goiter); we centrifuged systematically all sera following coagulation. Hemolytic sera were not used. By means of glass pipettes 1 c. c. was pipetted in diffuse daylight into small test tubes of ordinary glass and identical color, identical lumen and identical thickness of wall as the test tube of the standard; for each new serum another freshly cleaned pipette was used. Test tube and pipettes were rinsed with water following usage, mechanically cleaned, laid in dilute hydrochloric acid solution for a time, washed with distilled water and alcohol, then dried with ether and warm air and kept closed with a clean cork stopper.

In an ordinary test tube previously treated in the same manner, we prepared the reagent in which we allowed 3 c. c. of a 30 normal potassium iodide solution (chemically pure) to drip in drops with shaking into 5 c. c. of a 30 normal silver nitrate solution (chemically pure), immediately before any precipitation was formed, we pipetted off several c. c. of this mixture and then allowed 0.5 c. c. reagent to be added in drops to 1 c. c. of serum with careful mixing. The test tube was then closed with a clean cork. We now lighted with 400 candles at a distance of 25 cm. for exactly 20 minutes and then added 0.5 c. c. of a freshly prepared 25 per cent hydrochinon solution (dissolving of 0.25 gm. crystallized hydrochinon in 1.00 Aq. dest.), mixed again and then took readings every 5 minutes for a half hour. At the beginning we made a reading after ¾, 1, 2 and 3 hours, but for the most part the reaction was at an end after one-half hour. The mixing always took place with test tube closed with cork, never with finger pad closing, owing to the possibility of the disturbing influence of sweat colloid. All reagents, silver nitrate, potassium iodide, hydrochinon, were kept in dark brown bottles to protect them from decomposition with light. The pipetting off was always performed with diffuse day light; in the mid periods (following the pipetting off, between the readings during the reaction in progress) the sera was placed in a dark case. At the beginning we tried to carry out everything in the dark

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room but this was not successful; the pipetting could not be performed exactly enough in the red light and above all reading, which we made with the aid of Sahli's hemometer (left Kollargol standard, right serum), was impossible with red light. We needed an extremely intense light with the markedly browning sera and so we used the 400 candle transformer as source of light for the reading. In this way the periods during which the sera were exposed to the day light or artificial source of light (reading) were exceedingly alike; during the intervals the sera remained in the dark.

Of each serum, according to the amount, 2 to 4 reactions taking a parallel course with one another, were undertaken and the arithmetical mean taken as result. If the individual tests were too markedly divergent, the experiment was suspended and new tes prepared. All sera were always examin on the same day for the most part betwe 4 and 7 o'clock in the evening; the veno blood of the arm was in general removed b tween 8 and 10 o'clock and the goiter veno blood between 9 and 12 o'clock, mornings.

The following accounts of results proce from cases which were treated in the wa described above. In about half of the case only after the termination of the experimer did we know from whom the sera originated in the other cases a knowledge of the case wa not to be avoided before commencing th reaction; we made an effort, however, t remain objective as much as possible. Late the result of the rat and of the gas exchan experiment was always known to us at onc

(To be continued)

Practical Therapeutics

Mammary Extract in Menorrhagia

IT has been generally recognized that during the development of organotherapy some animal tissues have been used in which a definite endocrine function has not been established. The undoubted therapeutic effects have justified their use and it has been assumed that from such tissues there may be obtained active chemical compounds exerting a positive pharmacological effect, but playing no essential part in normal physiology. The very powerful substances derived from the post pituitary lobe, one a marked pressor and the other an oxytocic, are examples of this. The mammary gland is another, although yielding derivatives much less active pharmacologically.

Mammary substance has had a somewhat limited use in medicine; nevertheless it has persisted and its use has been repeatedly described in the journal literature and in some of the textbooks. The incentive to search for evidence of physiological function exerted by such substances, however, always remains, for it seems difficult to believe tha the organism elaborates chemical compound capable of exerting powerful selective actio on various physiological mechanisms, an that these compounds play no part in gener physiology.

The use of mammary extract in me orrhagia has not been constantly successf but there has been sufficient evidence to b lieve that it has some therapeutic value i various states of uterine bleeding. H. Vign (abstract below) has suggested most of th several theories used to explain the action mammary substance. All of the mechanism considered by Vignes appear to be insufficien to explain the action of mammary substanc

This action of mammary suggests a pos sible relation of mammary to corpus luteum Such a relationship has been suggested an the changes in the mammae at the menstrua periods and during pregnancy have been re lated to the corpus luteum.

The corpus luteum initiates remarkabl changes in the growth of endometrium befor

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menstruation and is apparently necessary for the building up and organization of the uterine mucosa before a menstrual period. The influence of the corpus luteum increases from the period of ovulation (10th to 15th day) up to a few days before menstruation. It then rapidly degenerates and the follicular hormone (Allen-Doisy hormone) dominates up to the period of ovulation of the next cycle when the new corpus luteum begins its period of influence on the new cycle as above. If (as in pregnancy) a corpus luteum persists and continues its development menstruation and ovulation are inhibited. Leo Loeb has shown these effects experimentally — the corpus luteum inhibits ovulation and proliferation of the vaginal epithelium. Others (Corner and Allen) attribute to the corpus luteum a hormone which induces progestational proliferation of the endometrium and Parkes shows experimentally (mice) that corpus luteum is necessary for the whole gestational process (up to the time of normal degeneration of corpus luteum of pregnancy).

Papanicolau, Pearl and Surface, Payne, Van Peenan and Cartland have shown the presence in the corpus luteum of a hormone which exerts an inhibiting influence on estrus and menstruation, and Parkes and Bellerby and others have assumed that in pregnancy the corpus luteum gives rise to an estrous inhibitor action.

Now if we accept as true the effect of the corpus luteum on the whole process of gestation, proliferation of the uterine mucosa and the process of estrus (and this seems undoubted even if our knowledge is not complete) we can conceive of a mechanism through which mammary extract may act in controlling uterine bleeding for the relationship of the corpus luteum to the mammae has been described by numerous authors (Leo Loeb *et al.*) and it is possible that there may be a reaction of corpus luteum to these extracts. In any event the subject of mammary opotherapy is a suitable field for further investigation.

Mammary Organotherapy. — H. Vignes. (*Bull. gén. thérap.*, 178 : 439, Dec., 1927.)

The function of the ovary determines modifications in the mammary glands each month, which increase in case of pregnancy; these changes are therefore a part of the preparation for pregnancy; they consist in more or less intense congestion and more or less active division of the cellular elements. The phenomena observed are, of course, of ovarian origin. That this is so has been demonstrated by the possibility of reproducing the congestion and cellular multiplication by injections of folliculin, by the determination of analogous changes in the castrated male guinea-pig following ovarian grafts, finally by the association of castration with an atrophy of the mammary gland.

Amenorrhea is sometimes associated with secretion of milk. In certain cases of false pregnancies with amenorrhea and abdominal obesity, an abundant secretion of milk has been observed. Certain amenorrheic young girls, apparently normal otherwise, lose an abundant quantity of milk each month for several days. Secretory outbursts have occasionally been observed at the menopause.

Painful mammary hypertrophy is often caused by ovarian disease without amenorrhea. Leriche published the case of a woman of 37 years with very painful hypertrophy of the breasts since puberty and menorrhagia at the same time. A laparotomy was performed and two large tubo-ovarian cysts were extirpated. Following the operation the breasts decreased in size and pain disappeared.

Dysmenorrhea often has an effect on the mammary gland and Dalché even notes a comparative frequency of mastitis and adenomas in such cases.

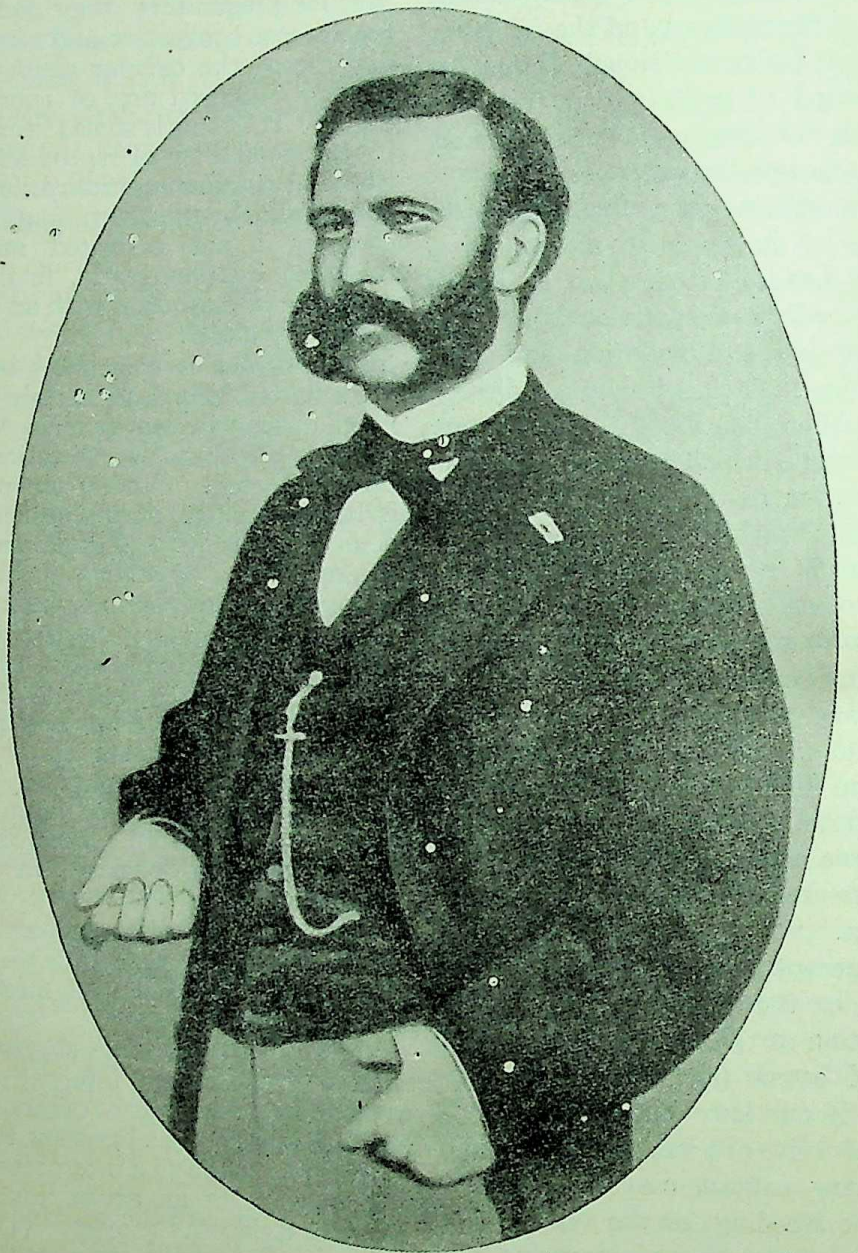
Certain authors have suggested the existence of a mammary internal secretion: the results of mammary organotherapy have especially served as basis for this hypothesis. Certain facts may be interpreted as being the consequence of an action exerted by mammary function on the ovary: (1) Many women do not menstruate during the months of lactation and it is among these that the majority of good nurses are found. (2) The suppression of lactation speedily brings on menstruation. (3) The fertility of nurses is lessened during the whole period of lactation.

(*Concluded on page 41*)

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The Doctor's Page



JEAN-HENRI DUNANT
(1828-1910)

The Red Cross Society has attained such renown and its services have been so universally accepted, that the stormy background of its origin and the tedious process of organization are almost lost to us. The founder of the Red Cross Society, Jean-Henri Dunant spoke significantly when, after the work of the society was well started, he said, "I sh

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retire into the background; the work is well under way; I am but a tool in the hand of God." Dunant desired always to be an unidentified volunteer worker unless the cause he essayed required that he associate himself with the illustrious family or the social rank to which he belonged.

Dunant was born in Geneva, May 8, 1828, in a noteworthy family consisting of five children, of whom the youngest, Pierre Louis, was to become a well-known instructor of Hygiene at Geneva; a father, Jean-Jacques Dunant, who held several important posts in the city and was active in public welfare work, and a mother, Anne-Antoinette Colladon, also of a distinguished lineage. One relative, Daniel Colladon, was the physicist known for his investigations on the transmission of sound under water and more especially for the invention of compressed air drills which made possible the opening of the Alps to the railroad.

With these inspirations before him, it is scarcely to be wondered that Jean-Henri contributed also to the already resplendent family name. As a child he was extremely solicitous of the welfare of others, and thoughtful of all those about him. He was always helping the less fortunate people in life, and gave much of his time to educating and teaching the inmates of the prison on Sundays. The slavery question, especially in the phases presented by Harriet Beecher Stowe so attracted his attention that he wrote an essay "L'esclavage chez les Musulmans et aux Etats-Unis" (1863, Geneva).

For a livelihood Dunant chose commercial occupation, but for a hobby he pursued studies in archeology, ethnography and history. While engaged in business in Algiers and Tunis he wrote a treatise "La régence de Tunis," a scholarly study of the history, government, finances, judicial system, naval affairs, climate, and people of Tunis, well supported with authoritative references. This work obtained for the author recognition in several learned societies and especially a membership in the "Société d'ethnographie" in Paris.

During the struggle of 1858-59, for the unity of Italy, in which France, Austria and Italy were intensely involved, Dunant chanced to be traveling in Southern Europe. Just after the battle of Solferino, June 24, 1859, he was at Castiglione, where the charitable inhabitants were helping to clear away the remains of the several armies, both wounded and dead. The awful gruesomeness of the battlefield, the inadequacy of the military medical service and the agonies of the wounded struck him so forcibly that he at once set himself to guide the group of voluntary workers to render first aid. It was not long before the cognomen of "Monsieur Blanc," by which name Dunant was called because of the white uniform he wore, spread far and wide. It is particularly significant that he made no distinction in the treatment of the wounded, whether Italian, French or Austrian — they were "all brothers." As a result of these experiences Dunant wrote "Un souvenir de Solferino" which achieved world fame and in which may be found the seeds of the idea of the Red Cross Society.

Herein Dunant depicts in great detail the clash of "two belligerent armies" and the disaster they leave behind them. He questions "Would it be possible to establish in every country of Europe aid societies whose aim would be to provide, during war, volunteer nurses for the wounded, without distinction of nationality"? Such a society would begin to function as soon as war was declared. "Societies of this kind . . . should obtain the favor of the authorities of the countries where they are created, and beg in case of war, from the sovereigns of the belligerent powers the permission and facilities necessary to carry out their purpose. . . . The moment of commencement of war the committee would call on those persons who desire to dedicate themselves, for the time being, to this work, which will consist in helping and nursing, under the guidance of experienced physicians . . ." ("Un souvenir de Solferino" translated by Mrs. D. H. Wright, 1911, Philadelphia). Later a clause was inserted into these principles which stated that the society "could be of great help in epidemics or great disasters such as conflagrations and floods."

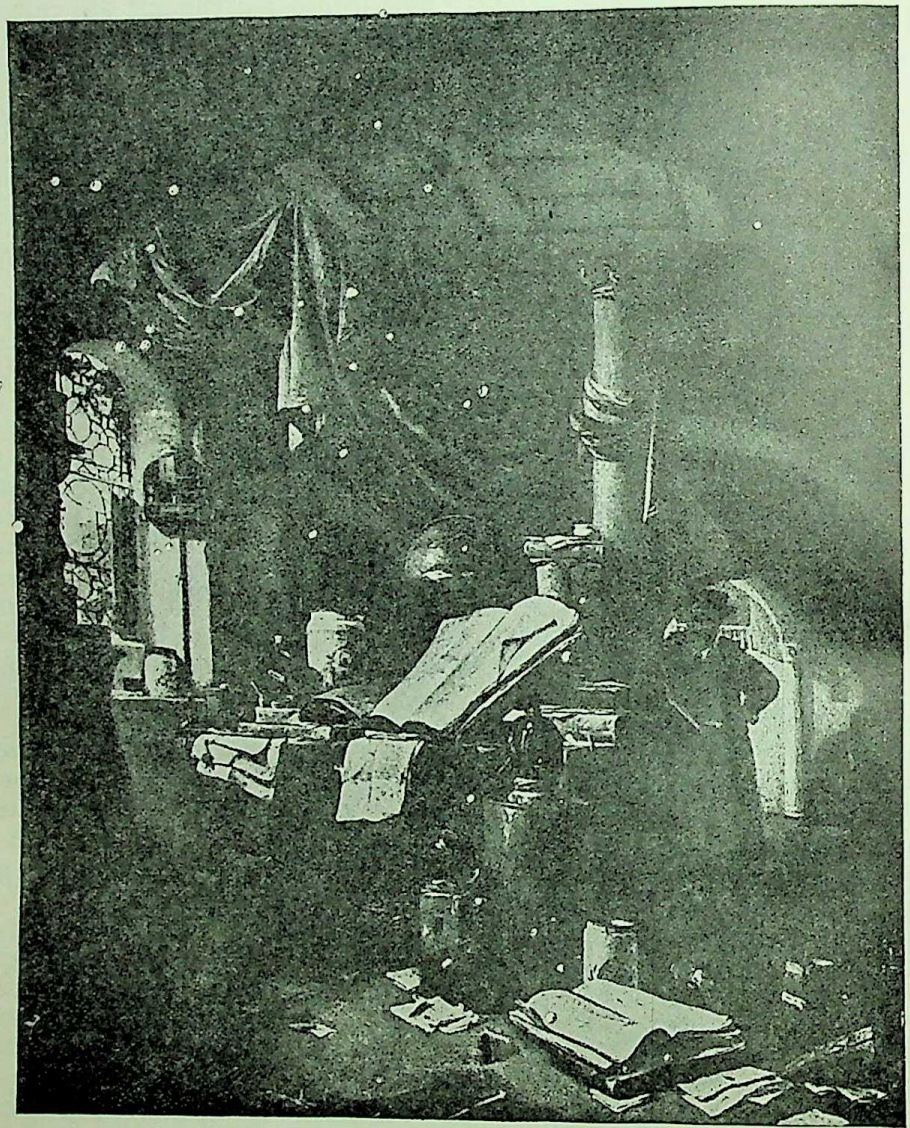
On February 9, 1863, the "Société genevoise d'utilité publique" appointed a committee to prepare the way for such a society, and made Dunant its Secretary, in which capacity he rendered not only official but also personal services in the cause he had inaugurated. He was favorably received by Napoleon III, Crown Prince Frederick and Queen Augusta as well as by other famous personages. The work of this committee

(*Concluded on page 48*)

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Medical Subjects by Famous Masters



"THE ALCHEMIST'S LABORATORY," by Thomas Wijck (1616-1677)

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Editorial Comment

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Hyperinsulinism

THE term hyperinsulinism is occasionally encountered in the literature. Usually it is applied to those conditions of hypoglycemia in which a blood sugar considerably below normal is not attended with the usual symptoms of such a condition. The number of cases which display this phenomenon is rather large and a satisfactory explanation has not yet appeared. The theory of excessive insulin production is purely conjectural, with almost no experimental work to support it. Most of the untoward symptoms of excessive insulin dosage have been attributed to the resulting hypoglycemia. Yet, a sufficiently large number of cases has been reported in which the symptoms were not at all, or only slowly relieved by administration of sugar and it seems clear that the degree of hypoglycemia frequently does not parallel the symptoms. Excessive insulin dosage produces not only marked lowering of blood sugar but may also apparently induce some toxic symptoms not necessarily dependent upon the hypoglycemia.

The relation of lowered blood sugar unassociated with symptoms can not at the present time be ascribed to excessive insulin production.

The use of the term hyperinsulinism by John (abstract below) is limited to the effects of insulin overdosage. While it is not established that insulin treatment tends to restore the function of the pancreas to elaborate insulin, the fact is well known that insulin dosage may be frequently reduced. It is possible that the substitution effect of administered insulin gives a rest period to the defective pancreas and spontaneous regeneration may occur. Hyperinsulinism (apart from administered insulin) as a clinical entity has not been proved.

Hyperinsulinism. — H. J. John. (*Surg., Gynec. and Obstet.*, 44 : 190, Feb., 1927.)

The term hyperinsulinism is employed to indicate a group of symptoms which are caused by a prolonged overdosage with insulin.

When a diabetic patient is placed on a certain insulin dosage, the amount being just sufficient to control his hyperglycemia and glycosuria, it does not follow that this dosage should be maintained during the whole course of treatment. The amount of insulin may have to be increased as time passes, or it may have to be decreased. If the endogenous insulogenic function of the patient improves and more endogenous insulin is provided, then less exogenous insulin is needed. In such a case the daily dosage of insulin which was prescribed at first becomes an overdose, and, if it is continued, symptoms of either mild or severe hyperinsulinism may appear. Because of the striking similarity of these symptoms to those of hyperthyroidism, a wrong diagnosis may easily be made and the patient subjected to a thyroidectomy without securing any relief from his symptoms. Therefore, hyperinsulinism should always be ruled out by a blood sugar examination, if hyperthyroidism is suspected in a patient who is being treated with insulin.

The treatment of hyperinsulinism is simple — merely the discontinuance of insulin. If

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this be insufficient the administration of some food between meals will be effective. Voracious hunger a few hours after the administration of insulin usually indicates hypoglycemia.

Urinary examination alone is not a sufficient basis for judgment in a case of diabetes in which insulin treatment is employed. In such a case if the patient happens to have a low renal threshold he may continue to eliminate sugar even in the presence of hypoglycemia. Without a glucose tolerance test such a condition might be interpreted as due to insufficient insulin dosage, and the insulin treatment would be continued and the dosage might even be increased, a course which would inevitably lead to hyperinsulinism.

Insulin and Hypoglycemia. — Editorial. (*J. Am. Med. Assn.*, 89 : 971, Sept. 17, 1927.)

The most noticeable feature of overdosage with insulin is the resulting hypoglycemia. The widespread custom of making estimations of blood sugar for diagnostic purposes has brought to light the fact that hypoglycemia is by no means as uncommon as has been assumed. Some observers have been inclined to attribute many of the instances of hypoglycemia to what they designate as hyperinsulinism. However, it is questionable whether hypoglycemia and hyperinsulinism are invariably closely interrelated. Harrop has demonstrated that the administration of carbohydrate to unconscious persons in insulin reactions does not always have the immediate prompt effect that has been anticipated. The degree of hypoglycemia apparently does not accurately determine the severity of the reaction, nor does the administration of sugar always relieve it. Recovery of consciousness may occur spontaneously even when the blood sugar is at a low level of concentration. Harrop regards it as probable that the toxic effects noted, especially the marked mental disturbances, may be due partly, or in some cases entirely, to some other action of insulin. These are possibilities that need to be recognized.

Thyroid and Growth

FREDERICK HAMMETT has made a number of substantial contributions to our knowledge of growth and the thyroid gland. In the article abstracted below he discusses the differential development of organs following thyroid and parathyroi removal. In this study he has compared th development of organs (the weight is taken a the measure) with body weight in animals i which both the thyroids and the parathy roids have been removed. These values hav been plotted graphically. If the curve for an particular organ coincides with the curve o the body weight at any given point, there is n distortion of development. If it deviate there has been a differential value in develop ment. Hammett has found that the lack o growth following thyroid and parathyroi removal is the result of essential under-nutri tion and not of any specific glandular effect o growth.

"Hence the conclusion is justified tha the difference in degree of growth response o the several organs in conditions of thyroid an parathyroid deficiency is, in general, due t specific organ constitution and the relatio of this to the metabolic or nutritional leve and not to any specific influence of glandula activity as such in the growth of the individua structure. Such is the essential basis of th distortion of differential development."

These conclusions are essentially in con cord with those of Child in his theory o "axial gradients." Child conceives that a various points along the long axis of the bod there is a series of differing metabolic rate These points of mere qualitatively increase metabolism give rise to differences of deve opment with a result which is qualitative organs are formed by reason of the increase cell division and development contingen upon the differences of metabolic rate.

Child's experiments, however, were mad on animals rather low in the animal scal (planaria) and it seems that in higher form there is finally a stage of embryonic develop ment in which the potential organs are inher ent in certain cells or groups of cells. (Loe has shown that the germinal area of a left le may be transplanted to the right side bu still develop as a left leg.) It is these primi tive areas and embryonic organs that exhibi

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the individual differences of reaction to the general metabolic stimulant — thyroid secretion. These differences are well described and charted in the article by Hammett.

Generalizations from the Differential Development Observed in Conditions of Thyroid and Parathyroid Deficiency. — Frederick Hammett. (*Am. J. Physiol.*, 82 : 250, Oct., 1927.)

Distortion of differential development follows both thyroid and parathyroid removal. With the exception of the hypophysis, the submaxillaries, and possibly the spleen, this is not due to any specific relation of glandular functions to organ growth, but to the general metabolic disturbance induced by the deficiencies.

The growth of some organs is more resistant and that of others is more sensitive than that of the body as a whole. The basis of this differential reaction lies in the relation of the metabolic processes of the organs in question to the bodily economy as a whole. The distortion is consistent in direction and produces a distinctly modified type of structural organization.

Since it can justly be assumed that endocrine activity in general is largely concerned with the regulation of metabolism, it is not improbable that the incretory organs have been and indeed still are endogenous participants in the determination of evolutionary change in the organisms in which they are present.

Abstracts

Surgical Treatment of Goiter. — G. E. Aróstegui. (*Revista Méd. Cubana*, 37 : 1082, Oct., 1926.)

Goiter in all forms is becoming more frequent in Cuba. Colloid goiter of adolescence or congestions of the thyroid require prolonged medical treatment. All the other forms of goiter are exclusively surgical and require the cooperation of the internist for a prolonged pre-operative and post-operative medical treatment. The assistance of the laboratory technician for pre-operative and histological examinations is also requisite, pre-operative examination being indispensable in the preparation of the patient and histological, in the following up of operative treatment (as in some of the author's cases) with deep radiotherapy.

Non-toxic goiters are exceedingly benign and very easy to extirpate. Toxic goiters require the attention of a genuine specialist and the whole cooperation of the hospital staff.

Lugol's solution is a two-edged sword and should be used only by a specialist. It has, to be sure, within a short time reduced the number of interventions in cases of hyperthyroidism. Hitherto, the interventions numbered three or four, whereas today only two interventions, and at times only one, are practiced.

Ten cases of goiter were subjected to operation by the author within the last three months.

Classification of Acromegaly in Two Clinical Forms: Simple and Complicated (with Optico-Diencephalic Symptoms). — C. P. Waldorp. (*Semana Méd.*, 33 : 765, No. 38, Sept. 23, 1926.)

Following a detailed description of the benign and malignant forms of acromegaly, as established by Prof. Oskar Hirsch of Vienna, the author relates his own experiences in seven cases of acromegaly, five of which were subjected to deep radiotherapy. He concludes that:

1. The clinical classification of acromegaly (disease caused by eosinophil adenoma of the anterior lobe of the pituitary) in the benign and malignant forms proposed by Prof. Hirsch of Vienna, is the equivalent of maintaining the existence of two distant entities in a single disease, with or without the participation of the optic routes. The malignant character would be given by the existence of symptoms of compression of the optic pathways and would be frequently accompanied by the symptoms proper to the syndrome of adiposogenital dystrophy. (Fröhlich-Babinski Type). In Hirsch's opinion, cases of malignant acromegaly should be operated upon early.

The author's classification of acromegaly is clinically broader and he divides his cases as follows:

(a). Acromegaly without optico-diencephalic symptoms (simple acromegaly).

(b). Acromegaly with optico-diencephalic

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symptoms (complicated acromegaly), cases in which there may be: exclusive or predominant symptoms of alterations of the optic pathways or of the diencephalic centers (adiposo-genital dystrophy, polyuria, glycosuria, disorders of sleep, etc.).

2. With the exception of special contra-indications, the treatment to be given is, in the author's opinion, the following:

(a). In simple acromegaly (without optico-diencephalic participation): irradiation of the pituitary tumor, with radiotherapy pursuant of the old technique of Béclère, and pluri-glandular organotherapy adapted to each case, and if indications of syphilis exist, corresponding combined treatment. If the course of the disease is not arrested thereby and if symptoms do not subside, deep radiotherapy.

(b). In acromegaly with optico-diencephalic symptoms, the conduct which the author follows is this: if the case is of recent origin, deep radiotherapy; if three months have transpired without improvement of the visual field or regression of the diencephalic symptoms, he advises hypophysectomy by endonasal route. If superaggregated symptoms of the disease persist or recur after the operation, the author believes deep radiotherapy an urgent necessity.

In those cases in which the destruction of the pituitary has reached a maximum, great vigilance of the endocrine-vegetative system is required, in order to prevent the so-called pituitary cachexia.

Gynecomastia in the Male and Its Relationship to the Whole Constitution. — F. Prange. (*Arch. f. Frauenkunde u. Eugenetik.*, **12**, Nos. 1 and 2, 1926.)

In seven cases of gynecomastia the great variation of the sexual types and the multiplicity of the constitutional relationship of this intersexual phenomenon were pointed out. Its etiology must be sought in part in a peculiar hormone effect, which however, must meet with a heightened developmental preparation of the rudimentary mammary gland hereditarily fixed in the germ plasm, when a gynecomastia is to result therefrom.

Adiposity and the Ovaries.—H. Wintz. (*Zentr. f. Gynäkol.*, **50** : 964, 1926.)

The author made an exhaustive study of the relationship between ovarian function and obesity. After the menopause, as well as following castration in younger women, the appeared in the majority of cases a lower of the basal metabolism, which frequently w accompanied by the laying on of fat. Admini tration of organotherapeutic preparatio led almost always to a rise in basal metabo rate and corresponding loss of weight. Ovari preparations were for the most part sufficie in other cases a pluriglandular preparati (thyroid, ovary) had to be utilized.

Metabolism Regulation. III. Contr bution to the Nervous and Endocri Influence on the Transformation Fat in the Liver.—E. Wertheimer. (*Pflüge Arch. f. d. ges. Physiol.*, **213** : 287, 1926.)

In the investigation on the regulation the transformation of fat in the liver, t following resulted with regard to the acti of the endocrine glands.

Insulin accelerated the transformation fat in the liver; at the same time an increa in glycogen content took place. Also follo ing adrenalin administration a marked tra formation of fat could be demonstrated the liver, whereas simultaneously new ca bohydrate was formed.

Hypoplasia of the Genital Glands an Insufficiency of the Thyroid. — Stang nelli. (*Riforma med.*, No. 2, 1926.)

The author directs attention to a disea picture which has received little considerati which makes its appearance at the age puberty, is associated with ascites, but mu not by any means be mistaken for a tuberc lous peritonitis. Essentially it appears infantile individuals with manifest hyp plasia of the genital organs and insufficien of the thyroid, who present the characteris symptoms of status thymico-lymphaticus a in whom the abundant lymph consequent endocrine disturbances appears as sero effusion into the abdominal cavity. In su cases, therapy has to curb the activity of t thymus gland and of the lymph system a has to strengthen the thyro-genital syste through the administration of gonad a thyroid extracts together with the oth hormones.

Thyroid Therapy.—A. Oswald. (*Terap contemporanea*, **1** : 507, 1926.)

A broad field opens today for thyro therapy. It is indicated in the treatment myxedema in all its forms, in endemic creti

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ism, at least in the form of thyrohypoplastic cretinism, which one can very well call endemic myxedema, as well as in the treatment of myxedemoidia, i. e., the aborted form of myxedema. Hypothyroidism represents a significant quota for thyroid therapy, with thyrogenous constipation, adiposity, chronic metrorrhagia, pregnancy nephritis, tendency to edema in pregnancy, edema of the menopause, psychic disturbances in the puerperium and in the menopause, hypothyroid cardiopathy, ulcerous dermatitis, if the manifestations should make their appearance in acne, furunculosis, chronic eczema or trophic disorders of teeth, hair and nails.

In the cases enumerated thyroid therapy is not only a substitution therapy but also a stimulative therapy, in which often the favorable effect of the treatment outlasts the suspension of thyroid therapy.

A broader field of application for thyroid therapy is found in diseases which are based upon a disturbance of metabolism. To this belong conditions of asthenic anemia without nervous etiology, avitaminosis, chronic articular rheumatism, arthritis deformans, true anemias, in which iron and arsenic only with the help of thyroid therapy lead to recovery, and defective callus formation.

Finally, thyroid therapy accomplishes good results in general dystrophic infantilism, in senility and sometimes in ectopic testicles and cryptorchidism, in reducing cures, true nephroses and edema of extrarenal origin, and in goiter (diffuse, parenchymatous and colloid) without Basedowian symptoms.

Contraindications to thyroid therapy are Basedow's disease, hyperthyroidism of every form, marked lability of the vegetative nervous system, decompensated heart failure, tuberculosis, chronic nephritis and severe diabetes.

In myxedema, one can, comparatively speaking, administer large doses: 0.2-0.3 thyroid desiccated substance once daily. In mild cases of myxedema, half the above dose once daily is sufficient, or the same (larger) dose every two days. If the appearance of hyperthyroidism is to be feared, it is well to administer only half doses every two days.

This dosage is also satisfactory for the symptomatic application of this therapy. In no case should the above given limits of dosage be overstepped, unless in reducing cures, under the supposition that the heart is sound and the vegetative nervous system is not overtasked. Then, double or triple the previously mentioned dosage may be given (two to three times daily 0.2-0.3 thyroid desiccated substance). The author advises against higher doses.

During menstruation the treatment should be discontinued. If symptoms of hyperthyroidism appear in the course of a treatment, the cure must be suspended and should first be continued after complete disappearance of the hyperthyroid symptoms with smaller doses.

Thyroid therapy must be continued for a long time. As a rule one obtains better results with small, long continued doses than with large doses continued over a shorter period of time. In complete myxedema treatment must be continued throughout the patient's lifetime. In hypothyroidism, the disappearance of hypothyroid symptoms sets a limit; in the symptomatic cures, the appearance of the desired effect of thyroid therapy. In recurrence of the disorders the treatment is again to be taken up.

Clinical Observations and Metabolic Investigations following Treatment with the Water-Soluble Folliculin. — Joseph. (*Archiv f. Gynäkologie*, 132 : 192, 1927.)

The author reports his experiences with folliculin in 20 cases. Five of these patients were amenorrheic for years — 2 to 8 years — and had already been treated without success with many ovarian preparations. In two patients transplantation of one ovary had been undertaken but with negative result. Moreover, two youthful patients who had been subjected to extirpation of the adnexa with conservation of the uterus, were likewise treated with folliculin; 8 patients with dysmenorrheic complaints and six more young patients who had been subjected to total extirpation for carcinoma.

Of the five patients with amenorrhea for years, menstruation again made its appearance in four, after an average of six weeks. Folliculin was injected daily. In one patient the structure of the uterine mucosa could be followed closely. Three weeks following curettage, the mucosa exhibited no change. Four weeks following initiation of folliculin therapy a definite growth of the glands, here and there also glycogen deposit was also demonstrated; again, after 3 weeks, regular gland epithelium with abundant glycogen

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content was to be determined. The patient now had regular menses. In one patient folliculin was without effect. The patient in whom the adnexa had been removed, had very severe symptoms of ovarian hypofunction, with an eczema intertrigo which could not be influenced by any special treatment (x-rays). Following twenty injections of folliculin the eczema disappeared; following the 28th injection the patient had a menstrual period lasting 2 days. In all 20 patients, the calcium content, blood sugar, cholesterin content and basal metabolism were examined regularly, at first before treatment and later following every 10 injections. In 13 of the 20 patients definite rises in calcium content were to be observed; the lower the calcium content at the outset of treatment, the greater was the rise. The increase amounted on the average to 2 mgm. per cent. In patients without rise in calcium content the clinical manifestations also remained uninfluenced.

In 15 cases a distinct increase in blood sugar was to be observed, most markedly following intravenous injection of folliculin. With regard to the cholesterin content a uniform action is not demonstrable. The basal metabolism changes in a favorable sense. In eight patients with very low basal metabolism a rise up to 40% occurred. On the other hand, in 6 patients with high basal metabolism it fell to 35%.

The Intestinal pH in Experimental Rickets. — Bernard L. Oser. (*Journal of Biological Chemistry*, **80** : 487, Dec., 1928.)

Bernard undertook experiments in order to examine the feasibility of the fecal pH test as a measure of vitamin D potency. Also, to study the relation of the hydrogen ion changes to the etiology of rickets.

He concludes that aside from its lack of specificity, it would seem that the fecal pH test for vitamin D potency fails to approach a quantitative ideal for these reasons: There is not sufficient uniformity in the reaction of the feces to permit the establishment of a border zone to distinguish between normal and rachitic rats; there is considerable fluctuation from day to day among individual rats in the fecal pH value, even while the diet remains unchanged; the time response of different rats to the experimental diets is not sufficiently constant.

As a qualitative indication of the presence of vitamin D the test is satisfactory provided other factors which influence the re tion (such as Ca:P ratio, acid:base ra inanition, etc.) are controlled.

The addition of acidogenic or alkaliger salts to the Steenbock and Black rickets-p ducing diet, in the amounts used by Zuck Johnson and Barnett was without effect either the promotion or inhibition of rick in these experiments. Although these s diets appeared to possess no influence on intestinal pH values not shown by unmodified basal diet, a positive effect greater proportions of the salts must not excluded.

The decreased alkalinity of the color contents of the normal rat is regarded related to phosphorus reabsorption whi normally occurs at that portion of the int tinal canal; whereas the sustained increa in alkalinity at this region in the rachi rat appears to be associated with inadequa phosphorus reabsorption. Since even t rachitic rat has been shown to absorb a utilize calcium to a certain degree, it is pr able that the primary etiological disturbar in rickets is the loss of phosphorus from t lower bowel, and the consequent decrease the level of this element in the blood plasm

Fasting, being accompanied by inadequa calcium intake, may affect recalcificati because of the conservation or restoration the inorganic phosphorus level in the bathi fluid of the bones.

Oser says in an addendum that followi the preparation of the foregoing, a paper Shohl and Bing appeared, in which simi conclusions are reached regarding the va of the fecal pH test in rickets. He adds t it is interesting to note their failure to redu fecal pH by irradiation of a modified Stee bock diet.

Pancreatic Function. — Seizaburo Ok da, Ehchi Sakurai, Tsunamoto Imazu a Kwanichi Kuramochi. (*Archives of Inter Medicine*, **42** : 270, Aug., 1928.)

The authors have devised a method ma ing possible a reliable and accurate estim tion of the pancreatic function. The patie used in the experiments were adults who h been under careful observation in the hos tal. Most of them showed only mild clini symptoms, such as constipation and neur thenia, and were thought to be free from pa creatic involvement.

By this method the enzymatic efficien for a fixed time is determined by multipl

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ing the degree of enzymatic activity by the amount of duodenal return collected. The authors, after considering the difficulties and failures, chose a three hour method, which seems most reliable. The normal value thus obtained from a study of 50 patients is from 30 to 120 kilo-units for trypsin, and from 50 to 300 kilo-units for amylase and lipase. The average value of the normal results becomes 70 kilo-units for trypsin and 140 kilo-units for amylase and lipase. Alcohol, ether, water and hydrochloric acid are applied as stimulants. Alcohol and ether stimulate the outflow at the beginning, but do not have a marked influence on the whole enzymatic efficiency in a three hours' collection, while hydrochloric acid seems to increase the output slightly.

The degree of enzymatic activity of the duodenal return collected in a short period gives but little information concerning the pancreatic activity. However, if the estimation is carried out fractionally every half hour or every hour separately for 3 hours, and the highest value is found, the result is fairly consistent, being over 500 units for trypsin and over 600 units for amylase and lipase. Age seems to have some influence on the enzymatic efficiency; it is highest between the ages of 20 and 40, and is somewhat less before and after those ages. The influence of sex is more obvious, the enzymatic efficiency being much less in the female sex. The amount of the duodenal return does not seem to be influenced much by age in patients from 16 to 62 years old. The influence of sex is apparent, the amount being much less in females. The amount of pigment ranges widely. It is judged that the amount of the bile pigment increases with age and shows higher values in the male sex.

Rôle of the Thyroid and Parathyroid Glands in Vaso-Motor Reflexes. — Swale Vincent and J. H. Thompson. (*Journal of Physiology* (London). **66**: 449, Dec. 20, 1928.)

These authors have endeavored to investigate the parts played, if any, by the various endocrine glands in the body in relation to vaso-motor reflexes and associated phenomena. This paper deals with their experiments relating to the thyroid and parathyroid glands in particular.

Decerebrate cats in which the thyroid and parathyroid glands are removed show after a certain lapse of time an abnormally large pressor response upon stimulation of skin, muscle or intestine. The authors describe two crises which may occur. Under certain conditions this abnormality can be combated successfully by the injection of parathyroid extract (Collip), and also by double adrenalectomy.

Reasons are advanced to show that the increased pressor response is due to liberation of large quantities of autacoid substance and is not owing to any depression of the vaso-motor reflex. The authors consider the secretion of this autacoid substance to be stimulated by some substance liberated by the adrenal glands, and that one of the functions of the parathyroid glands (and possibly the thyroid also) is to limit the secretion of autacoid pressor substance by control of the aforesaid stimulating agent.

A Non-Specific Pressor Principle Derived from a Variety of Tissues. — J. B. Collip. (*Journal of Physiology* (London), **66**: 416, Dec. 20, 1928.)

Collip describes a method for the production of extracts containing a powerful pressor component, a wide variety of tissues being used as a source.

The pressor extract derived from the prostate gland has been found to be essentially different in character from pressor extracts obtained from other tissues studied.

The non-specific pressor substance has an interesting pharmacology.

(a) It does not affect blood sugar.

(b) The pressor response is enhanced by small doses of ergotamine. A large dose may cause reversal of the pressor action.

(c) The pressor effect is antagonized by the intravenous injection of small amounts of cocaine hydrochloride.

(d) Atropine does not affect its action.

(e) Nicotine does not diminish the pressor effect but may cause enhancement.

(f) Small amounts have little or no effect upon isolated intestine, uterus or heart. Large doses are depressant.

(g) The pressor response (both height and duration) is directly related to the size of dose within certain limits.

(h) Repeated injections at short intervals do not alter the character of the pressor response.

Whether the active principle exists as such in the tissue, or is produced during the process of making the extracts, is not established.

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Relation of the Endocrine and Vegetative Nervous System to the Production of Disease in the Skin. — Harvey P. Towle and J. L. Grund. (*New England Journal of Medicine*, **199** : 1267, Dec. 20, 1928.)

Dermatologists are becoming slowly convinced that in disturbances of the endocrine system or in disturbances of the vegetative nervous system may often be discovered the foundations on which subsequent disease has developed.

John, who has studied the carbohydrate metabolism in hyperthyroidism, states that there is no specific dextrose tolerance curve for hyperthyroidism but thyroidectomy lowers the total metabolism and in consequence improves the carbohydrate tolerance. He, moreover, believes that hyperthyroidism plays a fundamental etiologic role in the disturbance of the endocrine equilibrium which constitutes the diabetic syndrome. Patients with hyperthyroidism, in whom a frank diabetic condition of severe type is not present, but merely a mild degree of disturbance of the carbohydrate metabolism, John considers to be functional diabetics. To these patients the administration of thyroid is not without danger.

Usher examined 106 cases of eczema of which he found that 54.7% had some degree of disturbance of the carbohydrate metabolism. Rabinowitch obtained about the same figures in a study of 713 non-diabetics. Usher found 40.5% of his eczematous patients had a delayed assimilation with or without a diminished carbohydrate tolerance as compared with 20% in a non-eczematous group. When considered in conjunction with John's studies, Usher's acquire added significance.

From the work of these two men it is seen that hyperthyroidism favors carbohydrate intolerance (John); that carbohydrate disturbance favors eczema (Usher); that in the presence of such disturbance, the skin reactivity is often increased; and that bacterial activity on the skin is favored in direct proportion to the amount of sugar in the sweat.

In view of the frequent administration of ovarian extracts it is interesting to know that in a study of 150 cases of various functional disturbances of the ovary Hornung found that the ovary did not regularly exercise any direct influence either on the basal metabolism or on the specific dynamic action of food stuffs.

Effect of Insulin on the Distributi of Non-Protein Nitrogen in the Blood. Stanley E. Kerr and Vartan H. Krikoria (*Journal of Biological Chemistry*, **81** : 4 Feb., 1929.)

The authors, in view of Sokhey and Alla report that insulin causes an increased exc tion of nitrogen in the urine, deemed it wo while to study the effect of insulin on non-protein nitrogen compounds of blo Recently it has been demonstrated th insulin causes a decrease in the amino ac nitrogen of blood; also, that the decrea in the amino acid nitrogen of the whole bo is entirely accounted for by a correspondi increase in urea.

The authors' experiments were perform on dogs fasted for 24 to 48 hours. Two tab are given. The first shows the effect insulin on distribution of non-protein nitro in blood. The results show a decrease amino acid nitrogen, with a correspondin larger increase in urea nitrogen. Sokhey a Allan's results suggest that the increa excretion of nitrogen after insulin might due to a breakdown of protein for the sak glucose formation. This hypothesis wo suggest that the production of urea should increased in proportion to the fall of bl sugar, and to the length of time the hy glycemia is maintained. To test this hypo esis, in three experiments shown in ta two, the blood sugar and the amino and u nitrogen were followed in whole blood 7 to 9 hours. In two of these experim the urea not only showed no increase, definitely decreased, contrary to the res obtained in the ten other experiments. Th results indicate that the formation of ure not dependent upon the level to which bl sugar falls, nor upon the duration of the hy glycemia. The dosage of insulin liker seems to have no influence on the amoun urea formed. The results suggest either t the low level of blood sugar is not itself stimulus which causes the increased cata ism of nitrogenous material, or possibly t the nitrogenous reserve is limited in quant as otherwise prolonged hypoglycemia sh cause a greater increase in urea. It has b suggested that the extra nitrogen excre after insulin has its origin in a reserve "deposit protein" which may be depleted fasting. Possibly this reserve may be me the free amino acids of the tissues.

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Antirachitic Potency in Relation to Volume of Oil in the Liver of the Cod. — Alfred F. Hess, Charles E. Bills and Edna M. Honeywell. (*Journal of the American Medical Association*, **92** : 226, Jan. 19, 1929.)

The authors found that, contrary to current opinion, antirachitic potency varies inversely with the amount of oil in the liver of the cod. From extremely poor livers, oil was extracted which was 200 times more potent than high grade cod liver oil, and far more potent than any oil heretofore assayed. Oils from the livers of individual cod may vary 1,000 times in their antirachitic value.

Treatment of Diabetes Insipidus with Pituitary Posterior Lobe Extract Applied Intranasally. — John R. Campbell, Jr., and Herrman L. Blumgart. (*American Journal of the Medical Sciences*, **176** : 769, Dec., 1928.)

The authors studied 8 cases in succession of diabetes insipidus of various etiologies. Intranasal application of posterior lobe pituitary extract was as efficacious as hypodermic injection in controlling the fluid intake and urinary output. The authors draw attention to the importance of inserting the cotton pledget soaked with pituitary extract high in the nasopharynx.

Some Clinical Aspects of Hypothyroidism. — A. H. Gordon. (*Canadian Medical Association Journal*, **20** : 7, Jan., 1929.)

Gordon presents a group of cases having the common factor of diminished thyroid gland activity, but in their external appearances showing dissimilar clinical characters.

Perhaps the disease most commonly confounded with hypothyroidism is pernicious anemia. Chronic nephritis is the disease most likely to be mistaken for myxedema. Mental disturbances, especially of the depressed type, are sometimes associated with hypothyroidism. Pericarditis with effusion, secondary anemia, migraine and a case of on-coming cardiac pain and weakness have been observed and are reported.

When starvation, hypopituitarism and Addison's disease can be excluded, persistently low basal metabolic rates usually mean hypothyroidism, but in the present state of knowledge it is unwise to make this diagnosis on the basal rate alone. The consideration of myxedema raises a number of issues. Fahr describes a type of heart which he believes to be due to myxedema. He describes also a type of electrocardiogram associated with it. At any rate a damaged heart in myxedema may hold its own with the low basal rate and consequently lessened work, but with thyroid medication, which acts in the same manner as exercise, the inefficient organ may reveal its inefficiency by giving rise to symptoms. It is necessary, therefore, to proceed with great care in thyroid therapy when any evidence of cardiac damage exists. It is in the lesser grades of hypothyroidism that symptomatology becomes vague and diffuse. Dysmenorrhea in young women, recurrent colds with asthenia, fleeting pains, and many other conditions, have been attributed to hypothyroidism. The pathology of hypothyroidism is essentially the story of the degeneration of the thyroid gland, which many now regard as a sequel of adolescent goiter. Usually the damage is permanent and treatment is for years or forever.

Two methods of treatment are the massive and the gradual. In the former there is given a dose of gland substance calculated to raise the lowered basal rate to normal as rapidly as may be; the other is a slower method with fractional dosage. Having in mind the cardiac dangers resulting from a suddenly elevated basal rate, one should consider the gradual method in subjects of vascular damage and those in the later ages, but in all instances, with the commencement of thyroid therapy, rest should be advised. Thyroxin, as a substitute for thyroid substance, may be given in the proportion of 0.3 mgm. for each unit of lowered basal rate, but reaction to it is sometimes severe, and vomiting, collapse, generalized pains, and anginoid pains may result. Broadly speaking, 0.3 mgm. of thyroxin corresponds to 5 gr. of thyroid extract.

Gordon has never seen a case of hyperthyroidism restored to complete health, either by medicine or surgery, nor a case of hypothyroidism return to an absolute normal. However, miraculous results are achieved by appropriate therapy.

Effects of Substances Other than Carbohydrate in Relieving the Toxic Symptoms of Insulin. — Julius J. Selman and S. Frank Weinman. (*American Journal of the Medical Sciences*, **176** : 865, Dec., 1928.)

The authors offer a preliminary report of the effects of substances other than carbohydrate, administered orally to cases of

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diabetes mellitus with symptoms of insulin overdosage. Five of six of these patients showed complete and prompt symptomatic recovery. Four recovered following the administration of mineral oil and one following the oral administration of pure protein. The authors do not give any explanation of these results but are contemplating further work in the hope of discovering the mechanism involved.

An Electrocardiographic Study on 123 Cases of Diabetes Mellitus. — J. Hepburn and Duncan Graham. (*American Journal of the Medical Sciences*, **176** : 782, Dec., 1928.)

In a series of 123 diabetic patients 56 showed serious electrocardiographic abnormalities at the beginning of diabetic treatment and that in a very fair percentage the electrocardiograms returned to normal after the diabetic condition was controlled by treatment.

It would appear from these observations that in the cases in which the electrocardiograms returned to normal after the diabetic condition had been controlled that the abnormal electrocardiograms had resulted from the effect on the myocardium of the perverted metabolism present in diabetes mellitus. Whether this is a direct action on the myocardium or an indirect one resulting from disease of the coronary arteries, or both, is difficult to answer. If one considers first the possibility of a direct effect on the myocardium, it may be stated that none of the few cases of severe acidosis studied showed an abnormal electrocardiogram and that many severe diabetics with hyperglycemia had normal electrocardiograms. As hyperglycemia and the products of the perverted metabolism present in diabetes mellitus apparently do not produce a direct effect on the myocardium resulting in an abnormal electrocardiogram, the possibility of an indirect effect from disease of the coronary arteries appears more likely.

In a discussion on the relationship of arteriosclerosis to diabetes mellitus, Joslin has clearly shown the effects of present methods of treatment of diabetes mellitus on the clinical course of this disease and has stressed the importance of the prevention and control of vascular disease in diabetes mellitus. In considering factors responsible for the development of vascular disease at an early age in diabetes mellitus, he has suggested the high percentage of fat in the diabetic diet as a cause. In the series of cases reported in this paper all the patients received diets containing the same percentage of fat. The results show that with the diet prescribed the normal electrocardiogram remains normal and the abnormal tends to improve.

When the vascular changes leading to death in diabetes are considered it is found that they are chiefly, if not wholly, confined to the intimal coat of the vessel, whether it be in the arteries of the heart, brain, kidney or lower extremity. Further, the early intimal changes are inflammatory in type, degenerative changes being secondary and appearing later. It is generally believed that no single factor is responsible for these changes in the intima. Yet there is general agreement that infection is the most important single cause. It may be that in diabetes mellitus the premature development of vascular changes is the result of infection acting in the presence of the abnormal metabolism of diabetes mellitus.

Insulin in Oily Suspension. — O. Leyton. (*Lancet*, **216** : 362, Feb. 16, 1929.)

More than a year ago Leyton came to the conclusion that some cases of diabetes mellitus with the usual typical thirst, polyuria, and hyperglycemia made a complete recovery provided they were treated with a fixed diet which supplied sufficient energy and tissue-repairing protein along with insulin, in doses which kept the concentration of the sugar in the blood below 0.15% throughout the 24 hours. In order to obtain this control of sugar in the blood some cases might require four or more injections of insulin during the 24 hours which made the treatment difficult.

It occurred to Leyton that it might be possible to prolong the action of an injection of insulin by delaying its absorption and thereby obtain the desired effect. He had a manufacturer supply him with insulin in an oil suspension and has used it in his private and hospital practice. He can give 90 units as a single dose, which will control the sugar in the blood just as well as 3 aqueous doses of 30 units each at intervals of 6 hours.

Diabetes Albuminuricus or Chronic Nephrosis.—Albert A. Epstein. (*New York State Journal of Medicine*, **28**: 1335, Nov. 15, 1928.)

The first and foremost manifestation of nephrosis is an intense and persistent albu-

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minuria. The proteins present in the urine in albuminuria have been found to be identical with the proteins of the blood. Albuminuria, according to Epstein, in so-called nephrosis represents an active excretion of the serum proteins by the kidneys. Because of a change in the proteins, be it chemical, physical or biological, as a result of which the body is unable to utilize them for whatever function proteins serve, they are excreted by the kidneys as foreign substances in the same manner that the kidneys excrete any other foreign matter present in, or introduced into, the blood stream. Just as in diabetes mellitus the glycosuria results from the perversion of carbohydrate metabolism, so in this disease the albuminuria has back of it a perversion in protein utilization. To this fundamental process Epstein has given the name "Diabetes Albuminuricus".

An increase in the fatty substances is practically a constant finding. One of these fatty substances, the cholesterol, was studied intensively. The cause of the hypercholesterolemia is uncertain although there is no doubt as to the relation of the cholesterol content of the blood to the activity of certain glands of internal secretion as the suprarenal and the thyroid.

The basic disturbance of diabetes albuminuricus is a subversion of protein metabolism. The albuminuria, the loss of protein substance from the blood, the edema, the lipoidemia, the reduced basal metabolism and other evidences of tissue starvation, all result from this basic disturbance. The problem in the treatment resolves itself into three specific propositions.

1. To replace the protein loss of the blood plasma. 2. To compel the tissues to utilize the protein and incidentally to reduce the lipoidemia. Thyroid often aids in attaining this desideratum. 3. To reestablish normal metabolism. When high protein feeding fails to accomplish this the institution of thyroid is definitely indicated. It is to be remembered that the main purpose in the use of thyroid is to stimulate protein utilization. It does not aim to replace protein feeding which is fundamental in the treatment of this disease. The amount of thyroid necessary to reestablish normal metabolic conditions in myxedema is relatively small, but in diabetes albuminuricus the amount of thyroid or thyroxin necessary to produce a therapeutic effect is most extraordinary. Daily doses of from 1.0 to 4.0 grams of thyroid are often required over long periods of time to elicit a metabolic response. While experience teaches that uncomplicated cases are susceptible of complete cure by the intelligent and persistent use of the high protein diet and thyroid therapy, it must be remembered that 6 months to 2 years may be necessary to accomplish this result. The presence of complications not only alters the outlook, but necessitates modifications of the therapeutic procedures.

Hyperthyroidism in Primary Hyperplastic Adenomatous and Colloid Goiters. — Hillier L. Baker. (*Illinois Medical Journal*, 55 : 111, Feb., 1929.)

The etiology of hyperthyroidism has been ascribed to many causes. Opinion at present seems to favor the view that in exophthalmic goiter the secretion is a perverted one, while in adenomatous and colloid goiter there is perhaps either an increase of thyroglobulin produced, or the thyroglobulin is not stored in the normal manner and the clinical entity described as hyperthyroidism is thus initiated.

In this series of cases of hyperthyroidism the exophthalmic or primary hyperplastic goiter made up 31% of the cases reported. The adenomatous goiter with hyperthyroidism made up fifty per cent. Colloid goiter with hyperthyroidism made up 18.7% of the cases reported. Of this number approximately 5% showed exophthalmos. Microscopically there is very little to distinguish the colloid goiter from the normal gland. It is the adenomatous goiter with hyperthyroidism which causes confusion as to the pathological classification of goiter; 40.5% of the cases reported in which exophthalmos was found were classified by the pathologist as adenoma. If, as Plummer believes, exophthalmos never occurs except in a gland showing hyperplasia and hypertrophy, these should be included in the exophthalmic group. There is a group of cases which show adenoma or an "adenomatosis" on re-operation. This finding has been present in several cases in which a primary hyperplasia was the finding at the first operation. The reason of adenomatous tissue in thyroid is not clear, but whatever the reason, adenomatous tissue is found in hyperplastic thyroids.

The incidence of hyperthyroidism in adenomatous goiter in this series of cases was most frequent during the ages of 21 to 40 years.

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The response to the use of iodin is similar in adenomatous and primary hyperplastic goiters and this factor raises a question as to their pathological difference.

The use of iodin, while beneficial causes an abeyance of hyperthyroid symptoms and does not result in cure. The improvement is temporary, and more apparent than real. The use of iodin should not replace the more safe and conservative polar ligations in severely toxic cases.

The Adrenal Factor in Hyperthyroidism. — G. W. Crile. (*Surgery, Gynecology and Obstetrics*, 48 : 371, Mar., 1929.)

The symptoms of hyperthyroidism are the same as the symptoms of adrenalism. The injection of adrenalin in a patient having hyperthyroidism produces an exaggeration of every symptom of hyperthyroidism. On the other hand, no amount of thyroid extract or of iodine can immediately cause any symptom of hyperthyroidism. Experimental evidence also confirms the clinical observation that as the thyroid activity is increased, the effect of adrenalin on the organism is stepped up in a sort of mathematical ratio. One fact alone is sufficient to show that the production of adrenalism is dependent on the thyroid, namely, that in myxedema the injection of adrenalin has little or no effect. In the presence of thyroid deficiency, adrenalin loses its power, but it is also true that in the presence of adrenal deficiency there can be no hyperthyroidism. Therefore, the thyroid and the adrenal glands are each equally essential to the production of hyperthyroidism.

The chief, perhaps the only, causes of thyroid crises are those factors that cause an increased output of adrenalin. The factors which cause thyroid crises are the following: pain, emotional excitation, foreign proteins, asphyxia, inhalation anesthesia, hemorrhage, and the injection of adrenalin.

The great role of the nervous system is shown by the following facts:

1. In hyperthyroidism, physiological rest is one of the most effective forms of treatment. 2. In many cases the cause of the disease can be traced to excessive nervous strain. 3. Ligation of the superior thyroid artery, which produces a break in the innervation of the thyroid gland, profoundly modifies the disease and usually converts a hyperplastic gland into a resting gland. To these should be added the following biologic facts: 1. That the disease occurs only in members of the human race, the principal characteristic of which is the development of the nervous system — especially of the brain. 2. That among the human race hyperthyroidism rarely occurs in the inferior peoples or in the stupid and criminal classes of the white race. All these facts indicate that the nervous factor belongs to the picture almost as definitely and potently as do the adrenal and the thyroid factors. The three dominant factors in the production of hyperthyroidism, therefore, are the thyroid gland, the adrenal glands and the nervous system.

The thyroid hormone causes a specific increase in the permeability of all the cells, hence an increased activity of the trillions of cells of the body. An important consequence of this specific action of the thyroid gland is an increase in the electric potential and in the electric conductivity of the tissues. Increased electric potential determines the range of the functional power of the organs and tissues. In myxedema both the conductivity and the potential of the tissues are exceptionally low, a fact in harmony with the clinical observation of the stupor and low metabolism of myxedematous patients — the opposite state to that in hyperthyroidism.

The thyroid cannot discharge the cells of the organs and tissues, the potential of which it builds up. The human, however, has a marvelous discharge mechanism which is entirely separate from the thyroid gland — the discharging mechanism is the nerve-adrenal combination. The active work — excessive work in hyperthyroidism — is due to the action of the nerve-adrenal mechanism. The thyroid mechanism is the charge-up mechanism; the adrenal-nerve mechanism, the discharge or work mechanism.

Thus, to recapitulate: 1. Nervous excitation is known to be a cause of many cases of hyperthyroidism. 2. Relief from nervous strain leads to relief of symptoms and the return of the hyperplastic gland to the normal. 3. In cases of hyperthyroidism the division of the nerve supply of the thyroid causes great improvement, sometimes even a complete disappearance of symptoms, and the return of the hyperplastic gland to the normal. 4. Every one of the known excitants of hyperthyroidism, namely, infectious diseases, focal infections, emotional excitation, etc., involves nerve excitation which in turn pro-

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duces an increased output of adrenalin. The adrenalin, in turn, has the power of activating the thyroid. In view of the above considerations it would appear that a primary adrenalectomy would have both immediate and remote advantages in cases of extreme hyperthyroidism.

Crile says that when one considers the correlation of the thyroid, the adrenals, and the nervous system it becomes clear that a new name must be given to the disease which has formerly been associated only with the thyroid by the term hyperthyroidism.

The Parathyroid Glands. — E. Larson. (*Clinical Medicine*, 36 : 170, Mar., 1929.)

From experimental and clinical evidence gathered by Larson, it would seem that the parathyroids are concerned in the maintenance of the normal level of the blood calcium.

That the parathyroids are concerned in detoxification of toxins absorbed from the gastro-intestinal tract has been a thesis supported by Dragstedt et al.

Medication in parathyroid deficiency may be of two types; treatment with calcium lactate, with lactose to increase absorption; and by the administration of parathyroid extract. The danger of overdosage with parathyroid extract should always be considered. Parathormone, subcutaneously, has proven beneficial in several cases. Snell treated a case of tetany, which did not respond to calcium lactate, with parathyroid extract and had favorable results. Hjort, in his report, stated that large doses of calcium lactate (5 gm. every 4 hours, day and night) were not very effective. Desiccated parathyroid substance was given in large doses (3 gm. daily — 166 times the ordinary dose) without any favorable influence. When parathyroid extract, 20 to 30 units daily, was administered parenterally, supplemented by oral thyroid therapy, a favorable influence was exerted. Several other cases treated by parathyroid extract have been reported. Replacement therapy by oral administration of either the fresh or desiccated glands has been of no avail, either experimentally or clinically. Desiccated parathyroid has been omitted from "New and Non-Official Remedies".

Allen, Compere and Austin found parathyroid therapy beneficial in the control of prolonged menstrual bleeding. Ogawa believes that it is helpful in promoting the calcification of fractures. Ross has demonstrated that removal of 3 of the 4 parathyroids definitely delays the union of fractures.

Repeated injections of parathyroid extract may lead to other disturbances than those produced by the hypercalcemia. Hueper has shown that they may lead to necroses in the myocardium, and in the cortex of the adrenal gland.

Pregnancy Complicating Simple Goiter and Graves' Disease. — H. Gardiner-Hill. (*Lancet*, 216 : 120, Jan. 19, 1929.)

Gardiner-Hill discusses the incidence, results and effects of pregnancy in simple goiter and Graves' disease from data obtained from a study of the histories of 115 married women suffering from these conditions.

Twenty-six were cases of simple goiter and 89 of Graves' disease. Of the latter, 71 may be classified as primary Graves' disease—patients in whom symptoms of intoxication had been present from the outset. The remaining 18 were cases of secondary Graves' disease in whom symptoms of intoxication had appeared after some years during which a simple goiter had been present. All but 2 of the 26 cases of simple goiter were sporadic. Twelve of these had originated primarily in adolescence and persisted into adult life, while the remaining 14 had developed in adult life. In all but two of this latter group the goiter developed originally during pregnancy or the puerperium. It would seem, therefore, that simple goiter, developing in adult married women at times other than these, is comparatively rare. In the majority of the cases the effect of pregnancy on the goiter was a further hypertrophy of the gland, and in multiparae the steplike enlargement which was found by Lawson Tait. In 2 patients on whom a partial thyroidectomy had been performed before pregnancy occurred there was a recurrence of the goiter during pregnancy. These patients also almost invariably developed symptoms of hypothyroidism in later life.

Of the 14 patients who had developed goiter in adult life, 6 had no subsequent pregnancy. Thyroid deficiency is often accompanied by sterility which can be overcome in a certain proportion of cases by treatment with thyroid extract. A considerable degree of thyroid deficiency was present in the majority of the cases after their first pregnancy and it appeared they had not received adequate treatment with thyroid extract. The development of goiter during pregnancy

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did not appear to have any harmful effect on pregnancy. The effect of pregnancy on the goiter was in nearly every case the same — i. e., a further hypertrophy of the gland. In later years the majority of these individuals developed well-marked symptoms of hypothyroidism.

In 8 of the 71 cases of primary Graves' disease the disease originally developed during pregnancy. In 6 this had no adverse effect on the pregnancy. In the seventh patient, although the pregnancy was carried to full term, the child was stillborn. The eighth patient miscarried at 3 months, very shortly after the onset of the disease. It may be concluded that primary Graves' disease developing during pregnancy in the majority of cases does not materially affect the course of the pregnancy.

The incidence of pregnancy in secondary Graves' disease was low, only 2 instances occurring out of 9 cases in which it was possible.

In the series of cases of primary Graves' disease the incidence of pregnancy was 50% of the possible cases.

In cases of Graves' disease the poor results of pregnancy — miscarriage or premature birth in 50% — may be attributed to shocks, mental stress, and inadequate rest and treatment, for where satisfactory conditions were attained and mental stress was absent the results were generally good. In the cases which relapsed after pregnancy there was more often than not a history of miscarriage or premature birth. On the other hand, when the pregnancy was carried to a successful termination, the improvement in the symptoms was generally maintained.

Hyperthyroidism Induced by Synthetic Thyroxin in a Patient Affected with a Pluriglandular Syndrome with Scleroderma and Cataract. — P. Sainton and H. Mamou. (*Presse méd.*, **36** : 8, 1928.)

Presentation of a patient who gave manifestations of thyro-testicular insufficiency. The patient was treated with thyroid and parathyroid preparations, with injections of hypertonic saline solution and finally with subcutaneous injections of synthetic thyroxin. Following one injection of only 5 milligrams the syndrome of hyperthyroidism made its appearance: tachycardia, tremors, psychic hyperexcitability, loss of almost 2 kgms. of body weight within 2 weeks, without glycosuria. These conditions correspond entirely to the symptoms called forth by the injection of organic thyroid extract. Great caution is, accordingly, enjoined with the use of thyroxin subcutaneously.

The Role Played by Disturbances of the Sympathetic Nervous System and of the Endocrine Glands in the Pathogenesis of Cutaneous Affections. — A. Lévy-Franckel and E. Juster. (*Urol. and Cutan. Rev.*, **30** : 327, June, 1926.)

Studies of the sympathetic nervous system have shown the possibility of perceiving the disturbances of the functioning of the nervous system in its regulatory effect upon the epidermis. Outside of its own proper action upon the cell and upon the cutaneous glands, the sympathetic system acts by its role as regulator of the circulatory system. The importance of the circulatory factor begins to come more and more into evidence. Another source of cutaneous impulse is the humoral impulse and particularly the hormonal. The blood which irrigates the skin contains the products of the glands of the economy, and notably of the endocrine glands, the action of which upon the morphology and the growth of the body is considerable.

The researches of endocrinologists have revealed numerous examples of the relationship existing between skin troubles and lesions of the endocrine glands. In like manner the clinical examination and laboratory tests — mainly basal metabolism — have made possible the demonstration of this hormone action in numerous cases of trophic cutaneous diseases. Also, the specific activity of the cells of the skin and of the cells of the cutaneous glands aside from all nervous or humoral action must be taken into account. Guillaume assigns to the cutaneous covering, considered as an organ, an antitoxic role in close correlation with the glands of internal secretion. Thus without wishing to make of the skin an endocrine gland it should be considered as susceptible of its own proper reactions corresponding with the particular status of its cells and of its glands. An analysis of the causes which regulate the proper functioning of the epidermis, of the epidermic products and of the cutaneous glands shows that these causes are the same as those which regulate the secretions in general.

The authors studied exhaustively certain cutaneous affections in regard to their rela-

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tionship with the endocrine sympathetic systems. In this group are the affections in which the role of the sympathetic and of the endocrine glands rests upon physiological bases. In most of these affections it is difficult to separate from a purely clinical point of view the action of the organo-vegetative system from that of the endocrine glands, and still more difficult to separate those due to the action of the sympathetic and those in which the dominant appears to be due to the para-sympathetic. Alopecia areata is among the affections with which the dermatologists see the connection with the endocrine-sympathetic. In the syndrome of the complete section of the peripheral nerves, hypotrichosis may vary from slight epilation to complete falling out of the hair. In hypertrichosis the role of the sympathetic nervous system and of the endocrine glands in the physio-pathology of hypertrichosis has been less disputed than the action of these two systems in the reverse phenomenon.

The role of the nervous system in the pathogenesis of hypertrichosis is all the more manifest since it is clearly demonstrated by physiology and the clinic. The part played by the sympathetic remains more obscure.

Pigmentary troubles may manifest themselves in the hair or in the skin. The influence of the nervous system upon the development of the nails is well recognized. The action of the nervous system and of the endocrine-sympathetic manifests itself equally in corneous patches. According to some authorities ichthyosis is of endocrine origin. Pilary keratosis, the authors have observed, accompanies a perturbation of the sympathetico-circulatory system (as in infantile paralysis). It may be under the dependence of a lesion of the endocrine system and in particular of the synergistic groups, the thyroid and the sexual glands. Seborrhea which seems to the authors to be more under the influence of the sympathetic nervous system and of humoral troubles (in the wide meaning of the word) than microbian infection, may be connected with an alteration of the endocrine system. Among the staphylococcic affections, a place quite apart should be reserved for acne. It is certain that the condition of the serum plays a role in its occurrence. Its frequency in women at the two extremes of sexual life suffice to prove this. The connection of acne with puberty and the menopause and the augmentation of basal metabolism in acne patients should suggest opotherapy in this affection. Kraurosis should be listed under the neuroglandular dermatoses. Pautrier admits the existence of an endocrine trouble as the origin of erythromelia. Bloch and Blamoutier have succeeded in obtaining notable amelioration in one case with polyglandular opotherapy.

The study of sympathetic reflex in adults affected with exfoliative marginal glossitis has shown the authors that there exist disturbances in the endocrine glands such as modifications of the pilometer and oculocardiac reflexes. The connections of limited desquamation with the sex-life of a woman, its frequence during the period of infancy corresponding with the development of the thymus, are interesting to notice. Milian and Perrin have made certain of the sympathetic pathogenesis of true dyshidrosis, not including dyshidrosiform epidermomycoses. The authors have twice observed that the occurrence of dyshidrosis coincided with a zone. In one of these two patients they discovered pilometer reflex disturbances. Raynaud's disease or symmetrical gangrene of the extremities is regarded as a sympathetic syndrome caused by the excitation of the vasoconstrictor nerves whatever the reason (exogenic, endogenic or endocrine) of the excitation. Erythromelalgia (Weir-Mitchell's disease) is a painful syndrome characterized by painful paroxysms. It is localized in the extremities, and is accompanied by redness, swelling of the integument, and local elevation of temperature. As in Raynaud's disease it is a vasomotor affection. Both are caused by an organic or functional perturbation of the medullary vasomotor centers. The endocrine dysfunction, particularly of the ovary adds an important factor in certain cases. Acrocyanosis of the hands of Brocq had been attributed by Marañon to an affection of the endocrine system (the hypogenital hand). In certain cases observed by the authors this influence was undeniable.

Psoriasis, eczema, urticaria, prurigos, pemphigus and pityriasis rubra pilaris come under the affections in which the role of the sympathetic nervous system and of the endocrine glands is based entirely upon therapeutic results.

The role of the sympathetic and of the endocrine glands rests only upon hypotheses in cases of naevi, Recklinghausen's disease, pruritus and lichen, erythrodermia and purpuras.

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Diabetes with Renal Glycosuria. — C. Voight. (*Lancet*, **213** : 916, Oct. 29, 1927.)

Among cases of true diabetes it is not unusual to notice certain ones in which the sugar tends to appear in the urine at either a high or a low level of blood-sugar concentration. Voigt reports an interesting case which illustrates the danger of an unrecognized low renal threshold to the successful control of diabetes by means of insulin.

In this case there is evidence that carbohydrates are not hurried through a rapidly emptying stomach; on the other hand, many processes in the gut will be modified by the want of the normal stimulus of acid leaving the stomach. It may be instructive to make gastric analyses in available cases of renal glycosuria, and to investigate renal threshold points of patients showing total achlorhydria.

Diabetic Acidosis without Ketonuria or Ketonemia. — Abraham Rudy and Charles M. Levin. (*N. Y. State J. Med.*, **27** : 1240, Nov. 15, 1927.)

The authors present this case because as they say diabetes may be discovered for the first time in old people and can be dangerous, contrary to common belief that the disease is mild in old age; also, this is another case of diabetic acidosis without the presence of acetone bodies in the urine and blood.

This is an instructive case of diabetic acidosis from which several important conclusions may be deducted. It proves the importance of a routine urinalysis in the acute case seen at home by the general practitioner as well as in his chronic cases. A positive sugar certainly does not prove that diabetes was the cause of this condition, at the same time the negative acetone does not exclude an acidosis.

The combination of all the symptoms together with the laboratory findings, gives the diagnosis. This case, as well as all the other cases of diabetic acidosis without ketonuria or ketonemia and also the experimental work on the acetone bodies, point to the conclusion that the acetone bodies are not always the direct or the only cause of diabetic acidosis resp. coma. The problem of diabetic acidosis must still be considered unsolved.

The authors conclude their paper as follows:

"A case of diabetes mellitus and acidosis discovered for the first time in a woman seventy-two years of age is presented. The problem of a diabetic acidosis without acetone bodies in the urine and blood is discussed and literature reviewed. A typical diabetic acidosis and its treatment at home are described."

The chemical methods used in making determinations were the following.

For

1. Sugar in the urine, the qualitative Benedict test.
2. Acetone and aceto-acetic acid in the urine, the qualitative Rothera test (a nitroprusside test).
3. Plasma sugar, the Benedict method.
4. Aceto-acetic acid and acetone in the plasma, the Wishart application of the Rothera test to the plasma.
5. CO_2-combining power of the plasma, the Van Slyke method.
6. Quantitative blood urea, Van Slyke and Cullen's modifications of Marshall's method.

The Rothera test is the most delicate test for diacetic acid and acetone. It is sensitive to one part of aceto-acetic acid in 20,000 while ferric chlorid reacts only to about one part in 8000.

Clinical Recognition of Pituitary Tumors. — Oskar Hirsch. (*Lancet*, **212**: 1339, June 25, 1927.)

Hirsch describes the ocular type of pituitary tumor and bases his observations upon about 100 cases of verified hypophyseal tumors upon which he has operated. A characteristic symptom is the visual disturbance without any striking constitutional disturbance. However, the patients nearly always suffer from some disorder of the function of the genital glands.

Thyroid and Parathyroid Bone Tumors without Primary Lesion of the Thyroid Gland. — R. Alessandri. (*Surg., Gynec. and Obstet.*, **45** : 35, July, 1927.)

Alessandri writes of the difficulties encountered when endeavoring to make a sure diagnosis between a simple goiter and a benign tumor. He studies the possibility of metastases in benign lesions of the thyroid gland (goiter and simple adenoma). In a recent paper he demonstrated that several cases which were reported as bone endotheliomas were really secondary tumors of thyroid (or suprarenal) type, often with seemingly benign primary lesions of the gland. Many hypotheses have been advanced to explain this behavior which does not conform to the ac-

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cepted doctrines of the pathology of malignant as compared with benign tumors and with the simple hyperplastic or degenerative lesions such as the so-called goiter.

The theory accepted with most favor is that which seeks to prove the possibility of embryonal aberrations and of the formation of foci of thyroid tissue in abnormal sites. These at a certain time of life, generally more or less late, can give place to structures with a progressive development of neoplastic type. It must also be taken into account that tumors may develop in accessory thyroids and metastasize, because the primary tumor can be easily overlooked and the thyroid gland in its normal site shows no enlargement. Accessory thyroid is to be found in the neck, at the base of the tongue, and in the mediastinum. The last two localizations are the most important as thyroid so placed is apt to be overlooked at a routine examination. There are cases in which no change of the thyroid gland is present, not the slightest enlargement. Alessandri has observed and operated on two such cases. He reports them because the thyroid gland did not show even the slightest change or enlargement before the onset of the skeletal growth, during its development, nor after the operations, which in both cases had to be repeated because of recurrences. Nothing which could possibly represent the primary site of an eventual tumor whence the metastases might have proceeded could be detected in the regions of the neck, of the tongue, or in the mediastinum where aberrant thyroid glands are usually found.

Persistent Thymus. — W. L. Denney. (*Can. Med. Assn. J.*, **17** : 89, Jan., 1927.)

A case is reported of an infant, aged 2 months, who was having attacks of cyanosis with difficult respiration. This difficulty was apparently neither of the pure inspiratory nor expiratory type but occurred in either phase. At each attack death seemed imminent. No history was obtainable. The temperature was normal and respirations normal between attacks. The infant was emaciated but not acutely ill. A diagnosis of enlarged thymus gland was made.

Five days after admission a Roentgen ray treatment was given. This gave immediate relief. Eleven days after the first treatment the child had one slight attack of cyanosis. One other treatment has been given and now at the expiration of four days there have been no attacks. The general nutrition of the child has improved and the weight increased.

The Carbohydrate Metabolism of Adrenalectomized Rats and Mice. — Carl F. Cori and Gerty T. Cori. (*J. Biol. Chem.*, **74** : 473, Sept., 1927.)

When rats surviving double adrenalectomy were subjected to a 24 hour fast, the liver glycogen disappeared and the blood sugar fell considerably below normal. In contrast to the liver glycogen, the glycogen content of the muscles of these animals remained the same as that of normal control rats fasted for the same length of time. The low blood sugar is linked with the lack of liver glycogen, since the muscle glycogen does not participate in blood sugar regulation. The absence of liver glycogen in fasting adrenalectomized rats is not the result of a disturbance in the synthesis of sugar into glycogen, since liver glycogen is formed at a normal rate when glucose is fed. Twenty-four hour fasting adrenalectomized rats absorbed glucose at a much slower rate than twenty-four hour fasting normal rats.

During 4 hours of glucose absorption the adrenalectomized rats without insulin oxidized 373 mg. of glucose and formed 270 mg. of glycogen (124 mg. in the liver and 146 mg. in the rest of the body). The adrenalectomized rats receiving insulin injections oxidized 471 mg. of glucose and deposited 37 mg. of glycogen in the liver and 185 mg. of glycogen in the rest of the body. The difference in liver glycogen of 87 mg. corresponds closely to the difference in glucose oxidation of 98 mg., while the glycogen deposition in the rest of the body (chiefly muscles) is not materially changed. The same results have been obtained previously on rats with intact adrenals, where a discharge of epinephrin in sufficient amounts to produce a metabolic effect could not be excluded. Since the adrenals were absent in these experiments, the conclusion has been drawn that the lessened deposition of liver glycogen and the increased sugar oxidation, also to be observed in insulinized rats with intact adrenals, are due to insulin alone and not to a combined action of insulin plus epinephrin.

Previous experiments have shown that insulin injections lead to a decrease in the liver glycogen of fasting insulinized mice. An identical result has been obtained on mice from which both adrenals had been removed 20

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to 30 days previously. The adrenalectomized mice without insulin showed 2.16% liver glycogen after a fasting period of 1 to 5 hours. The adrenalectomized and insulinized mice that were killed simultaneously showed only 0.79% liver glycogen. Since the effect of insulin on the liver glycogen of fasting animals is the same, whether or not the adrenals are present, there is no need to assume that epinephrin is responsible for the decrease in liver glycogen following insulin injections.

Action of Epinephrin upon the Cardiac Rhythm. — Harold L. Otto. (*J. Lab. and Clin. Med.*, **13** : 70, Oct., 1927.)

Since epinephrin by virtue of the powerful accelerator stimulation it induces can cause the appearance of cardiac arrhythmia, in many instances of a dangerous or unpleasant nature, it is distinctly advisable to administer it with caution particularly to cardiac patients or those individuals presenting a history of having had one of the cardiac arrhythmias.

Exophthalmic Goiter

(*Continued from page 10*)

"Eponymically, Parry's disease — and not Basedow's or Graves' disease — is the most appropriate designation for both toxic adenoma and exophthalmic goiter, for Parry was the first observer who described all varieties of toxic goiter.

"Clinically, a nodular goiter without exophthalmos may be as toxic or even more toxic than a smooth, diffusely enlarged, or exophthalmic goiter with pronounced ocular signs. The prognosis in a severe case of toxic adenoma with myocardial insufficiency is much graver than that in a moderately severe case of classic exophthalmic goiter in which the patient has markedly bulging eyes and a fairly intact myocardium.

"Although toxic adenoma may run as severe a course as exophthalmic goiter, its clinical manifestations are usually milder, and the surgical results are more satisfactory than in classic exophthalmic goiter.

"The more favorable surgical results in toxic adenoma are due not to any fundamental difference in nature from exophthalmic goiter but to a variation of a single disease: In exophthalmic goiter, generally the entire gland is diffusely involved in the pathologic process, while in toxic adenoma of the thyroid the gland shows one or several pathologic foci with intervening healthy tissue between the affected areas. Hence, generally, the symptoms are milder, and the surgical resection is more satisfactory than in exophthalmic goiter."

The existence of toxic adenoma as a separate disease entity can not at present be conclusively established. In view of the widespread references in the literature, however, and the constant reference to it in relation to exophthalmic goiter, it is well to consider the opinions of those who have most thoroughly studied it.

(*To be continued*)

1. Ginsburg, S., *Arch. Int. Med.*, 1929, xliv, 73.
2. Mayo, C. H., and Plummer, H. S., "The Thyroid Gland." Beaumont Foundation Lectures, Series 4, Mosby Co., St. Louis, 1926.

Obesity. — Maximilian Kern. (*Clin. Med. and Surg.*, **34** : 440, June, 1927.)

The present-day classification of obesity is as confusing as it is unsatisfactory. In most cases it is too broad to meet all requirements. The endocrine factor is not properly understood, and therefore is underestimated. On the other hand, basal metabolic reading are not a sufficient guide in the proper management of nutritional disturbances.

No matter how caused, obesity, in a medical sense, is generally a manifestation of a pathologic condition and just as much a disease as is cancer or any other condition which expresses itself in abnormal tissue growth. There are exceptional individuals who, though obese by definition are still not pathologic subjects. Climatic conditions, food used, and their general mode of living may affect the definition when applied to them. Brown and Keith have observed that the circulating blood and plasma volume, when compared with body weight, is less in obese than in normal persons. As a rule fat deposits are more abundant in regions where the circulation is poor. Strouse and his associates have shown that the obese tend to

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store rather than to burn fats derived from carbohydrates. There is also a discrepancy in the metabolism of proteins between obese and normal persons. There must be some constitutional factor — some diathesis or temperament-affecting metabolism and obesity, as it is known that the latter is not always the expression of a disproportion between the food intake and bodily expenditure. Grafe considers that in every case of obesity from overeating there is a constitutional factor involved and that the attempt to define two types of obesity does not conform to facts.

Obesity, either generalized or localized, is a well-marked part of the clinical picture observed in disturbance of the secretions of the thyroid, pituitary, gonads and suprarenals. Obesity is a predisposing or direct cause of diabetes, arterio-sclerosis, arterial hypertension, and cardio-renal disease. The medico-actuarial statistical tables show that every pound of fat above normal for age and height is reflected in a regular increase in the mortality rate; the most favorable rate, in fact, not being in those which show normal weights but in those whose weight is substandard.

Prepubertal obesity in children, when pathologic, may be a precursor of imperfectly developed sex characters and organs. Marañon recommends that obesity in children, with metabolism of five per cent below normal, should be treated by thyroid extract, and by ovarian extract in the case of girls. The treatment of obesity can at no time be carried out along specific lines, and may frequently be a hazardous undertaking. Without the proper consideration of all the factors involved, such as nutritional irregularities, endocrine disturbances, heredity and habits it may not only be unsuccessful but in many cases harmful. The most important changes arising from too rapid reduction of fat tissue are excessive production of fatty acids and acidosis. In mild cases of obesity, a loss of from 3 to 6 pounds per month should suffice. In cases of excessive obesity with cardiac decompensation, up to 30 pounds a month can be reduced without danger if the patient is carefully supervised.

Diabetes Mellitus and Myxedema: — Heber C. Jamieson. (*Can. Med. Assn. J.*, **17** : 88, Jan., 1927.)

The occurrence of glycosuria in the myxedematous patient has been noted, though the number of cases of diabetes mellitus with myxedema reported have been few. Wright reports two. In one the basal metabolism was −26, and in the other −28. An interesting case is reported.

A man, aged 37 years, presented all the classical symptoms of myxedema. Thirteen years before seen by the author, he was passing an excessive amount of urine. He suffered a gradual increasing weakness though his appetite increased. About a year before Jamieson saw him he lost his hair. Six months later he noticed swelling of his eyes, and his eyelashes fell out. Basal metabolism was −35 and −36. There was neither sugar nor acetone in the urine. In view of his history he was placed on a diet low in carbohydrate. His blood sugar before breakfast was 0.120%. Thyroid extract, 1 grain three times daily, was given. As long as he was allowed to become myxedemic he remained free from symptoms of diabetes. When thyroid extract was given and the basal metabolism approached the normal, all the classical symptoms returned. An attempt was made to solve the difficulty by giving small doses of the extract and small doses of insulin which resulted in improvement in his condition.

The Sensitizing Action of Alkalies. — A. Hemingway. (*J. Physiol.*, **62** : 81, Oct. 30, 1926.)

That the tone and activity of tissues containing plain muscle, such as blood vessels, intestine, uterus, etc., is largely dependent upon the acidity or the alkalinity of the fluids with which they are bathed has long been known. In addition to these changes in tone and activity there is considerable evidence that certain drugs are more effective when used in an alkaline medium. It has been observed that an exaggerated response to adrenalin accompanies the reaction to alkalies.

Pre-Operative Preparation of the Diabetic Patient, with a Discussion of the So-Called Diabetic Gangrene. — Edward H. Mason. (*Can. Med. Assn. J.*, **17** : 23, Jan., 1927.)

The well controlled diabetic is no more susceptible to infections leading to surgical complications than is the non-diabetic. Attention to details, minor details in the daily hygiene of the patient, however, should not be overlooked. Failure in this respect will

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lead to trouble. Prompt attention to small pimples and boils, cleanliness of the skin, and the daily hygiene of the feet, are measures concerning which instruction is due to every diabetic.

Most diabetics who develop surgical complications peculiar to their diabetic state fall into two classes: (1) young individuals who fail to live up to a strict dietetic regime, and (2) individuals beyond 50 years of age, who, either have a low grade diabetic condition of at least several years standing which has never been considered seriously, or patients who break their diet allowing themselves to have persistent hyperglycemia. Most major surgical complications including gangrene occur in patients of the first group of the second class, the most important complication being gangrene.

In most instances there is plenty of time to prepare a patient for operation but emergency cases occasionally are found. On the day of operation the patient should have a good fluid balance, some glycogen reserve, no ketosis, and an approximately normal blood sugar. Ten units of insulin given just before the operation is a wise procedure. The post-operative period is as important as the pre-operative. Freedom from glycosuria must be maintained if possible, and ketosis of any degree of severity prevented. This can be accomplished through diet, fluids and insulin. Vomiting once established dehydrates rapidly and will convert a mild ketosis into a severe one. The diet should be gauged according to the carbohydrate tolerance of the patient, giving fluids and soft food at the start. Milk as a sole food is not especially suitable for this period as it is relatively high in carbohydrate.

The major surgical complication of diabetes mellitus today is gangrene, almost always of the lower extremities. It usually develops in the untreated or poorly treated cases. Diabetic gangrene is now held to be due to arteriosclerotic changes. Insulin cannot change the arterial condition, but its control of blood sugar and local care will save many limbs. The quartz mercury vapor lamp is a valuable aid in these cases.

A System of Microscopic Tubules in the Thyroid Gland. — R. R. Fitzgerald. (*Can. Med. Assn. J.*, **17** : 542, May, 1927.)

Fitzgerald reports the results of his investigations which confirm the presence of a system of microscopic tubules in secreting epithelia and found in the thyroid gland. The microscopic tubules were demonstrated in normal thyroid tissue obtained at autopsy and in pathological material removed surgically. Tissue was prepared by the method described by Williamson and Pearse. When it is properly prepared by this method a new structure is seen in the epithelium.

The histological studies of Williamson and Pearse, extending and completing the work of previous investigators, seem to prove conclusively that two distinct secretory processes must be recognized in the normal thyroid gland. One is the relatively passive process resulting in the storage of colloid; the other is an active process resulting in the formation of a distinct product which is not colloid. Between these two separate phases there is an indifferent or resting phase. The appearance of the system of microcanaliculi varies in different parts of the normal gland according to the particular stage of physiological activity which happens to be present. In the colloid-storage phase they are drawn out to minute hair-like lines which are almost invisible. In the indifferent or resting phase they appear as thick black branching and communicating lines occupying a position near the center of the epithelial column. The resulting structures sometimes resemble giant mitotic figures. In the active secretory phase they appear as purple, almost transparent tubules filled with deeply chromatic coarse granules. The tissue of Graves' disease exhibits these structures in every vesicle. The so-called fetal adenomas, built of closely packed small vesicles, show well-developed microcapillary systems. In adenomas composed of colloid-containing tissue the microcanaliculi are absent, or are too fine to be detected by this method. The significance of this system of microtubules has not been established. Their association with the process of active secretion is constant and striking. They can only be demonstrated with great difficulty when the gland is in the stage of colloid storage, but they are constantly present, large, and contain granular material when the epithelium is in the stage of active secretion.

Bearing in mind the conspicuous presence of distended microcanaliculi in all actively secreting tissue it seems logical to suggest that they may be channels of absorption in which secreted material is collected from the interior of the acinus, conveyed outward through

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the layer of epithelial cells, and delivered to the lymph spaces outside the vesicle. However, when the neoplastic states are examined well-developed canaliculi are found in tissue in which the other characteristic features of secretory activity are lacking. If these distended canaliculi are the result of stagnation and passive distension by secretion unable to escape in the ordinary way on account of encapsulation, this observation would tend to detract from the theory that the microcanaliculi act as absorption channels for secreted substances.

Studies on the Action of Parathormone. — Wilhelm C. Hueper. (*Ill. Med. J.*, **52** : 393, Nov., 1927.)

Hueper examined the effects produced by the injection of excessive amounts of parathyroid extract on the organs of dogs. The clinical course observed in the animals did not differ in general from the description given by Collip. Study of the causes of the reported pathological alterations has to be based upon the knowledge of the physiological effects of the parathyroid hormone. Regulating the calcium metabolism it controls the acid-base balance of the cells and the body fluids and also the equilibrium of the tonus of the vegetative nervous system.

The parathyroid extract administered in physiological doses induces:

1. A prolongation of the systole and a shortening of the diastole of the heart through irritation of the pneumogastric nerve.
2. A dilation of the vessels of the internal organs.
3. An intensification of the tonus of the stomach and the intestine.
4. A rise in the calcium level of the blood.

Excessive amounts of the parathyroid extract produce by an exaggeration of the above noted effects:

1. A gradually increasing incompleteness of the diastole of the heart and a slow and irregular pulse resulting in a drop of the blood pressure and an impairment of the general circulation.
2. They induce an excessive intensification of the tonus of the stomach and intestine, causing vomiting and diarrhea.
3. They augment by the highly increased blood calcium the coagulability of the blood to such a degree that the formation of thrombi in the congested vessels becomes imminent.
4. They cause such a supersaturation of the blood with lime salts that these are precipitated in various organs interfering eventually with their proper functioning.

Injections of parathyroid extract administered in larger amounts and short intervals should not be given for therapeutic purposes without a continuous control of the blood calcium, because excessive doses of this hormone produce dangerous circulatory disturbances and calcifications in vitally important organs. Even injections of larger doses in intervals of 3 to 4 days to avoid accumulative effects are not absolutely harmless. This has been proved by recent laboratory experiments.

Hueper, in order to study the influence of the parathyroid hormone upon the production and calcification of osteoid tissues, fractured one leg in cats. At the end of the third week the callus of the treated cats exceeded in amount and degree of calcification by about 20-30% that of the control cats. Histological examinations of the fractured bones showed also a higher amount of newly formed bone and a higher degree of consolidation than was present in the control cats. Hueper says if further investigation should substantiate his present findings he would consider parathyroid extract as an eventually useful therapeutic in cases of delayed fracture healing and in the treatment of rickets. He calls attention to the following:

Dogs which had received injections of parathyroid extract and in which the blood calcium level was raised to around 15 mg. showed a markedly increased production of urine. The results of the investigations including histological examinations and findings and considering that the parathyroid hormone is a strong stimulant of the vagus nerve a beneficiary effect of this hormone in cases of oliguria or anuria, being the result of an acute glomerulonephritis or reflex anuria, is very likely. By relieving the vessels of the kidney from the excessive vasoconstrictory splanchincus tonus the hormone will effect the reëstablishment of a proper circulation and the subsequent secretion of urine and excretion of the retained waste products. Moreover, it will raise the blood calcium level which is frequently found to be low in glomerulonephritis and thereby arrest the irritability of the muscles. The regulating effect of the parathyroid hormone upon the activity of the heart may be mentioned too in this connection.

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A Case of Mongolian Idiocy, Occurring in One of Male Twins. — Gordon Chown. (*Can. Med. Assn. J.*, **17** : 943, Aug., 1927.)

A case is reported which supports the views of McLean, Halbertsma, Strauch, Mitchell and Downing that where Mongolism occurs in twins, it is the result of a double ovum pregnancy, and that the etiology is due to a defective germ plasma.

Herrman, while supporting this theory, goes further and states that Mongolism is a reversion to a primitive type, or in other words it depends upon the reappearance of recessive unit factors. The former view that the condition is due to exhaustion products: physical or nervous strain, syphilis, alcoholism, consanguinity, conditions operative during pregnancy, and endocrine imbalance, seems now to be refuted.

Xanthoma Diabeticorum: An Unusual Process of Involution. — Eli Goldstein and John Harris. (*Am. J. Med. Sc.*, **173** : 195, Feb., 1927.)

The authors describe an unusual case of xanthoma diabeticorum which showed a peculiar process of involution not mentioned in the literature. This occurred in a patient suffering from diabetes mellitus, to whom insulin was administered in the late stages of the disease. The consensus of opinion in the literature reviewed is that when the xanthoma nodules undergo resolution, they disappear completely or at the most leave a pigmented area over the site of the lesion. In the case here described three types of resolution went on simultaneously with little or no reference to the general condition: (a) the lesions on the palms disappeared completely; (b) those on the elbows coalesced and left large pigmented patches; (c) those on the legs and thigh underwent degenerative changes resulting in extensive scar formation — a process hitherto undescribed.

The Laryngeal Nerves: Their Relation to the Thyroid Gland. — Homer Dupuy. (*So. Med. J.*, **20** : 15, Jan., 1927.)

The author says "The thyroid problem is with us, and laryngology must be given the opportunity of enlightening the profession as to the pre-operative and post-operative status of the larynx." He says that this is necessary in order to know whether this organ is damaged by pre-operative pathologic changes in the thyroid.

Observations Based on 173 Consecutive Goiter Cases. — S. O. Black. (*Internat. J. Med. and Surg.*, **39** : 28, Jan., 1926.)

There are four varieties of congenital goiter: vascular, colloid, cystic, parenchymatous. The last mentioned is the most frequent; the cystic the least frequent, but when present may rival in size the fetal head. The colloid is very rare.

The vascular enlargement is not a true goiter. It results as a rule from the long labor incident to face presentation, and usually disappears within a few days after birth. The parenchymatous enlargement, if of a size sufficient to induce pressure, may cause the child to be dyspneic at birth, with cyanotic facies, periodic unconsciousness and a crowing sound on inspiration. This type of goiter will not occur provided the mother has a sufficient quantity of iodin during her parturient period.

The acquired goiter is more frequent than the congenital. It may be simple, toxic or malignant. The true cause of variation in thyroid function is not known. Many cases of hyperthyroidism date back to an acute tonsillitis. The gland is affected more frequently in the female than in the male. To every one soldier from the southeastern states, there were 15 from the northwestern with simple goiter, according to statistics of the World War. Kimball proved that hyperplastic and hypertrophied thyroids during childhood and adolescence were due to a deficiency in iodin. Thyroid enlargements have been eradicated in the public schools of Zurich, Switzerland, by giving a small dose of sodium iodide to the affected child each Monday morning.

All normal thyroids contain at least one-tenth of 1% of iodin; hyperplasia ensues when the amount is less. Adenomatous goiters contain iodin greatly in excess of the normal content. During pregnancy if the iodin supply becomes impoverished, the thyroid begins to enlarge automatically. Many multipara date the onset of their goiter to one or the other of their parturient periods. Should the expectant mother fail to get iodin her child might be born without a functioning thyroid, a cretin being the result. Any expectant mother developing parenchymatous enlargement of the thyroid should be given iodin salt at regular stated intervals to prevent goitrous offspring. Many children born with too little iodin have fetal adenoma in their glands, and

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these are apt to grow into adenomatous goiters, to become toxic, or to become malignant.

Cannon and Mix write of the interrelated physiology between the thyroid and the adrenal. They say that the adrenal is the whip to the thyroid, that it spurs the thyroid to greater activities during periods of emergency. Both these glands affect, through their secretions, the pulse rate, the pulse-pressure, and the respiration. The adrenal also throws into the blood stream additional quantities of sugar, to enable, as Mix states, the runner to increase his speed or the fighter his strength. The thyroid gland acts as the carburetor to the human machine, and through it the physiological elixir flows. Any glandular or secretory disturbance which results in the alteration of the chemical composition of its finished product, immediately disturbs one or the other of its functions. Hyperthyroidism often constitutes a problem for the internist and the surgeon alike. Frequently its symptomatology is such as to confuse it with paroxysmal tachycardia, neurasthenia, pulmonary tuberculosis and organic heart disease. Cannon states that thyroid function depends upon sympathetic nerve impulses. Mastin believes that the improvement following the ligation operation is due to an interruption of these impulses. All goiters, excepting small colloid ones, are potentially dangerous and should be subjected to early operation. It has been found that in the hyperplastic toxic goiter the administration of iodin is as efficient as the ligation procedure.

Practical Therapeutics

(*Continued from page 15*)

Proceeding from the hypothesis that an antagonism exists between lactation and ovulation it was supposed that lactation acted on the ovary and the genital sphere through the medium of endocrine products secreted by the mammary cell. Robert Bell recommended the ingestion of mammary substance in treatment of menorrhagias and even of fibromas as early as 1894. Various reports have been published concerning the efficacy of mammary organotherapy. On the basis of his observations in a series of 30 cases of menorrhagia or dysmenorrhea, Charlton concluded that the effect on menstruation if it exists at all, is not constant. The author possesses an extensive experience with mammary organotherapy. In a series of 15 cases of metrorrhagia or menorrhagia, treated with mammary extract, he had durable results in 7 cases.

If mammary extracts do exert a genuine therapeutic effect, even if inconstant, it remains to determine by what mechanism. It may seem plausible at first sight that the mammary extract acts as antagonist of the ovary. This explanation does not appear probable to the author for histological and experimental reasons. In two experiments in which he injected mammary lipoids into female guinea-pigs he found ovaries of normal appearance upon examination. Charlton demonstrated even more precisely that the extracts have no effect on ovulation.

Certain authors have spoken of an action on the uterine vessels. It is evident that a substance does exist in mammary extract which is capable of acting on the tonus of any vessel whatever. This vascular effect is, however, too weak and transitory to explain the effect of the medicament. An action on the uterine fiber has also been thought of. Fedoroff has noted that mammary extracts activate involution post partum. Scott and Ott have spoken of a myokinetic action. Adler, Schiffmann and Vystavel have obtained an atrophy of the uterus following prolonged use of the extracts. Cavagnis noted an increase in tonus which F. Spirito verified. But here also the action is slight and scarcely permanent and the author is not quite certain that this would suffice to explain the therapeutic effects obtained.

It is possible that mammary extract acts by an effect exerted through the medium of the adrenals. Adler, Schiffmann, Vystavel and Manzi have always observed in the course of their experiments that injections of mammary extracts in addition to their action on the utero-ovarian apparatus, occasioned a considerable hypertrophy of the suprarenal cortex and medulla. Such suprarenal hypertrophies are, however, too frequent following injection of organ extracts, to permit of a conclusion.

It may also be questioned whether mammary extract does not act on the uterine mucosa. This is an opinion which Adler has maintained, because having obtained abortions by the action of mammary extracts, he interpreted them as consequent to a disturbance of the terrain of nidation. No histologic evidence has been forthcoming in support of this hypothesis, however, which seems to merit further research, in the author's opinion.

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Practical Application of Our Present Knowledge of Calcium Metabolism. — A. T. Cameron. (*Can. Med. Assn. J.*, **16** : 759, July, 1926.)

The studies of Mellanby, McCollum and his co-workers have led to the identification of a new vitamin, fat soluble D, which is present in especially large amount in cod liver oil (also one of the chief sources of vitamin A). Hess has fractionated the oil, and obtained a non-saponifiable fraction soluble in acetone which is a thousand times more active than the original oil, and which is quite free from vitamin A. Butter contains much less of the new vitamin than does cod liver oil, milk a sufficiency for prevention, but not for cure of rickets, while egg-yolk is fairly rich in it. Of animal tissues bone-marrow is stated to be especially rich in it. It is not elaborated in the germinating seed as are several of the other vitamins.

Rickets, characterized by an incorrect and deficient calcification of bone tissue, can be produced in the young growing animal either by deficiency of calcium, or of phosphate, or of vitamin D in the diet. In the presence of an ample amount of the vitamin much smaller amounts of calcium and phosphate are sufficient to prevent rickets than when there is only a small quantity of D present. It conserves these mineral constituents in the body. In rickets there is found low serum calcium along with somewhat low serum inorganic phosphate, or low phosphate with normal calcium. In the former case the rickets may be accompanied by tetany. In rickets also there tends to be a negative calcium and phosphorus balance, owing to a continued loss of these elements from the body. In the normal growing child, bone requirements demand a marked calcium and phosphorus retention. Any digestive derangement which may upset the acid-base equilibrium may possibly, by affecting absorption of calcium and phosphates, lead to rickets. Acidosis is a frequent if not invariable accompaniment, and since acetone bodies are absent, it may be attributed to a mineral derangement. Incorrect dietary of the mother is probably a large contributory factor in nurslings. Rickets can be cured by cod liver oil, and by ultraviolet light. Direct sunlight contains sufficient of the ultraviolet rays to prevent onset of rickets, though perhaps not so readily to effect a cure. Clover hay made by exposure to sunlight is active; made in the dark it is inactive.

The curative effects of the ultraviolet rays can be produced by directly raying the child, or by raying a large number of different compounds and food mixtures which are subsequently fed. It seems extremely probable that the food-stuffs that can become activated all contain cholesterol or related sterols. Vitamin D is not cholesterol, but it is probably a related sterol. The rayed substance retains its antirachitic potency for several months, but apparently over-raying again changes it to an inactive modification. Roentgen rays and radium will not activate substances chemically related to vitamin D, and will not cure rickets.

One variant of rickets is accompanied by tetany, or latent tetany. Tetany occurs in the following conditions: rickets with tetany; infantile tetany of unknown origin; parathyroid deficiency through surgical or other causes; excessive thyroid feeding in rats; over-ventilation of the lungs; feeding or injection of sodium or potassium phosphate; feeding or injection of large amounts of sodium carbonate or bicarbonate, (and perhaps of other sodium salts); pyloric stenosis or similar conditions in which large amounts of hydrochloric acid are removed by vomiting or gastric lavage; occasionally in severe diarrhea; following injection of guanidine or methyl guanidine.

A normal degree of muscle and nerve excitability depends upon a balance of certain ions; an increase of sodium, of potassium, or of hydroxyl ions, and a decrease of calcium, of magnesium, or of hydrogen ions leads to greater irritability. It would appear that in all of the above conditions that lead to tetany its onset can be satisfactorily explained by a disturbance of the ionic ratio that governs muscle-nerve irritability. Most infantile tetanies, parathyroid insufficiency, and the tetany following sodium phosphate injection are definitely associated with a lowering of the blood serum calcium concentration. The others seem largely due to an increase in the hydroxyl ion concentration. Cameron emphasizes the probability that these tetanies result frequently from a combination of factors. He believes the tetany associated with guanidine is a purely pharmacological effect, not met in ordinary pathological conditions.

Collip has shown that the concentrated product of the acid hydrolysis of parathyroid glands, injected into animals in severe tetany following parathyroidectomy, quickly restores

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them to normal condition, at the same time raising their plasma calcium to normal level, and holding it there longer than the administration of calcium salts can do, whether these be given by mouth or injected. Such animals can be kept free from tetany for months, though, if injection of the extract be stopped, tetany recurs within a day or two. If the injection be given in large doses and at repeated short intervals the calcium of the blood is increased much above the normal level. When it is about twice normal other symptoms intervene, atonia, profound depression, anorexia, ataxia, vomiting, bloody stools, etc., and ultimately the animal dies. The same increased blood calcium, and ultimately fatal ending, follow injections of the extract into the normal animal. So far no antidote has been found for these effects from overdosage; evidently chemical control must at present be employed during the administration of the extract in clinical cases. These results have been confirmed by Macleod and others, including Moorhouse and Cameron. Cameron has showed that both the diffusible and the non-diffusible calcium are raised by this treatment — to approximately an equal extent — just as they are both lowered following parathyroidectomy.

Moorhouse and Cameron as a result of their studies with parathyroidectomized dogs have put forward a theory of the mechanism by which the blood calcium is maintained at a constant level. They believe that the parathyroids elaborate an internal secretion which controls the formation of a non-diffusible calcium compound in the blood, and that this, by a series of interlocked equilibria, keeps the diffusible calcium compounds of the blood to a constant ratio with itself. If the parathyroids function normally, the compound under their control will be kept at constant concentration and therefore the total blood calcium will remain constant. The slightly higher value for the plasma calcium of infant's blood suggests a more active parathyroid function. This theory, to be complete, must take into account the further control by vitamin D. While the administration of cod liver oil or of ultraviolet light restores blood calcium to normal in the rickety child with deficient blood calcium there is as yet no evidence to determine the nature of this control, though it seems to be closely interwoven with that of inorganic phosphate.

When calcium salts are given by mouth, or injected, it has been recognized for some time that there is merely a most transient effect on the height of blood calcium. Excessive doses produce only temporary benefit so it is easily understood why therapeutic doses can lead only to very transient results. The most that can be hoped for is continued slight benefit from moderate doses given at frequent intervals. The excess calcium may be, perhaps, in part secreted, but it would seem in large part to be deposited in the tissues, especially the bones.

Tuberculosis, rickets and various diseases have been associated with a disturbed calcium metabolism. However, accurate workers in tuberculosis seem to be agreed that no such disturbance is involved and that the administration of calcium salts is of no benefit. In epilepsy blood calcium is normal. This condition is not associated with parathyroid deficiency.

The types of parathyroid enlargement separately reported to accompany rickets in chickens, and to follow ultraviolet light treatment, merit attention, since, if such changes do occur, they tend to bring into alignment the actions of vitamin D and of the parathyroid secretion.

Diabetes: Reaction of the Diabetic Patient to Insulin. — Julius Jensen. (*Journal-Lancet*, **46** : 143, Apr. 1, 1926, and **46** : 170, Apr. 15, 1926.)

In this paper Jensen records observations in the treatment of about 200 cases of diabetes and glycosuria. Sugar-tolerance tests were extensively used in the investigation of the cases. He found them essential for diagnostic purposes and useful in illustrating the progress of the cases and thereby also giving an idea as to the prognosis. He thinks the best prognosis can be given in cases showing hardly any alteration of their sugar tolerance whilst under treatment; their diabetes seems to be of the stationary type that is not much influenced by any factors. A fairly favorable prognosis has been given in cases whose tolerance seems to show much improvement under treatment, but their condition is of a more fluctuating variety and therefore likely to fluctuate adversely when the patient is no longer under the care of the hospital. A distinctly unfavorable prognosis is of course given when the tolerance decreases in spite of treatment. Low sugar-tolerance curves were found on several occasions, often associated

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with hypoglycemia, and could almost always be explained by carbohydrate starvation in some form or other.

In order to obtain some experience of the immediate effects of insulin on the blood, 20 units of insulin was in 7 cases given before breakfast and the blood-sugar estimated at 15 minute intervals for 2 hours. The immediate effect was in most cases to produce a depression in the sugar curve. However, there are different degrees of sensitiveness to insulin in diabetics. Some patients become so easily hypoglycemic as to be thought hypersensitive to insulin. Most cases do well on 10 to 40 units a day; some require much bigger doses. Although the insulin dose often has to be diminished after a time, it is doubtful how far this is due to real improvement in the sugar tolerance or whether it is caused by an accumulation or late effect of the insulin. Jensen says that in no case of diabetes mellitus was it possible to demonstrate any definite improvement of the tolerance due to insulin. The insulin treatment was only found to be symptomatic for the defective sugar tolerance which is one of the manifestations of the metabolic disorder called, diabetes mellitus. These rather discouraging conclusions may, perhaps to some extent, be explained by the fact that these diabetics were chronic cases where material alterations were hardly to be expected.

Since the introduction of insulin hypoglycemia is much more frequently met with than previously. How far hypoglycemia occurs in normal persons is not known to Jensen. Diabetics may become hypoglycemic on starvation, on certain diets, and practically always on the administration of insulin. It is the insulin hypoglycemia which gives rise to symptoms. How far hypoglycemia due to other causes than insulin may give rise to similar symptoms is doubtful. There is a recognized mode of death in diabetes, called the diabetic collapse, which is supposed to be due to heart failure, and which to a certain extent resembles severe insulin hypoglycemia.

Various symptoms have been described as due to overdosing with insulin or as features of hypoglycemia. Jensen has noted three kinds of symptoms often difficult or impossible to distinguish from each other.

The very mildest symptom of hypoglycemia is a feeling of hunger. Jensen does not treat these cases except to add a few ounces of vegetables to the diet. If the hypoglycemia becomes more severe, it is often the mental symptoms that are predominating. There may be in some cases profuse sweating all over the body. The first stage may gradually pass into a second, where the patient becomes increasingly more drowsy. Later he cannot be roused and sinks into absolute stupor. Another definite group is the motor symptoms. In the first stage there is often a certain amount of trembling, fear and mental alienation. In the more severe hypoglycemia this gives way to a motor weakness; there is loss of control. At the height of an attack the patient presents a striking picture and if this state is allowed to go still further he will pass into stupor without any symptoms of motor disturbance. Motor symptoms may occur as the patient comes out of stupor. They then take the form of tonic contractions. On the whole the symptoms of severe hypoglycemia often show a tendency to severe asymmetry. Respiration which, in most cases, is shallow and rapid, may occasionally be deep and heaving.

Treatment is well known and simple and clinical improvement always takes place fairly rapidly after the administration of sugar. In the rare and more severe cases Jensen used adrenalin to increase the blood-sugar.

It is now recognized that, besides the beneficial effect insulin has on the various pathological features of diabetes, it may in itself give rise to a number of symptoms.

Some of these may be considered results of over-action on the recognized diabetic symptoms, as the changing of hyperglycemia into hypoglycemia, acidosis into alkalosis, etc., thus producing the symptoms associated with these conditions. Others can be described as direct toxic effects, either of the insulin itself or of the substances injected along with it.

Jensen observed acute local reactions in one or two cases. They were simply inflammatory swellings and required no treatment. Chronic reactions are small cutaneous or subcutaneous circumscribed, painless areas of fibrosis. They are especially noticed on the arms of patients who have been having insulin for some time. Often they make it difficult to continue the injections in the areas affected. If the area is rested and the injections performed elsewhere in the body the condition clears up after a few weeks.

Of all the complications met with in insulin treatment, the pains are the worst. The

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patient may get them from a few days to several months after he has started insulin. Two of Jensen's patients were doing fairly well on insulin treatment until the pains began. From this time their condition deteriorated. The pains may start in any part of the body, either in the site of the insulin injection immediately after it has taken place, or corresponding to a particular nerve, or some other part of the body, and they may spread to other parts of the body. In these generalized cases it has been the hands and feet that have been worst affected. The pain may last from one-half to a couple of hours or still longer, in some cases being constantly present. These latter cases deteriorate very quickly and it often becomes difficult to continue the insulin. In two cases Jensen was obliged to discontinue it. The milder forms yield to aspirin and other analgesics. Moderately severe cases do well on massage and electricity but severe cases remain refractory to all known treatment.

Effects of Partial Parathyroidectomy. — Frederick L. Gates and J. H. B. Grant. (*J. Exp. Med.*, **45** : 115, Jan. 1, 1927.)

Observations on the endocrine tissues of rabbits irradiated with a quartz mercury arc lamp have disclosed the striking hypertrophy of the parathyroid glands produced by the irradiation. Histologically, this hypertrophy was found to be a true hyperplasia of the endocrine tissue, but a study of the calcium and inorganic phosphate content of the blood of these rabbits failed to reveal any significant



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changes from the normal levels. The irradiation and consequent hypertrophy of the parathyroid glands, resulted in some degree of protection to the animals when part of the parathyroid tissue was extirpated. This fact indicates that the remaining hyperplastic tissue was potentially active, and that the increased factor of safety represented by this condition of the remaining tissue resulted in less loss of blood calcium, a more rapid initiation of recovery, and an absence of the rise in the inorganic phosphorus of the blood serum which was a characteristic result of partial parathyroidectomy in normal rabbits. A fall in calcium in all the irradiated rabbits, without a corresponding rise in phosphorus, shows that the drop in calcium is the primary reaction, and a rise in phosphorus a secondary reaction following parathyroidectomy. The relation of the rise in phosphorus to the development of tetany still remains obscure.

Course and Prognosis of Diabetes Mellitus in Children. — Gladys L. Boyd. (*Can. Med. Assn. J.*, **17** : 1167, Oct., 1927.)

The average length of life of the diabetic child has been lengthened by the use of insulin. Normal growth and development occur in the treated diabetic child. Diabetes in children is a rapidly progressive disease, which may not only be arrested in its course, but made less severe under adequate treatment with diet and insulin. The criterion of successful treatment consists in the absence of glycosuria and the maintenance of normal blood sugar for the greater part of the time. Fluctuations in tolerance are frequent, and gains may only be retained by fidelity to treatment. Pathological examination furnishes a certain degree of evidence, favorable to the belief that pancreatic regeneration may occur. The incidence of diabetic coma has not declined, but a material decrease in its mortality due first to insulin, and secondly to earlier recognition and treatment has occurred.

Effects of Injections of Calcium Chloride or of Disodium Hydrogen Phosphate. — Frederick L. Gates and J. H. B. Grant. (*J. Exp. Med.*, **45** : 125, Jan. 1, 1927.)

No significant differences were found in the reactions of irradiated, normal, or partially parathyroidectomized rabbits to injections of calcium chloride or disodium hydrogen phosphate. Intravenous injections of calcium chloride caused only a transient rise in blood calcium, which returned to its former level within a few hours. The upper level of blood calcium concentration is independent of parathyroid control. Subcutaneous injections of disodium hydrogen phosphate caused, in all three groups of rabbits, a similar depression of the blood calcium level. After large doses of the phosphate solution, all of the rabbits showed signs of acute tetany in which many of them died. Death or survival was not determined, apparently, by the absolute depression of blood calcium. The rabbits that died were those, in all three groups, in which a phosphorus retention carried the initial rise in serum phosphorus to even higher levels in the hours preceding death, and so changed the normal calcium-phosphorus ratio to a small fraction of its former value.

Effects of Inanition. — Frederick L. Gates and J. H. B. Grant. (*J. Exp. Med.* **45** : 139, Jan. 1, 1927.)

In these experiments the authors observed the effects of complete inanition in irradiated, normal, and partially parathyroidectomized rabbits to determine possible differences in the fasting metabolism of calcium and inorganic phosphorus with which the parathyroid glands, directly or indirectly, are so essentially concerned. No distinctions could be drawn between normal irradiated, and partially parathyroidectomized rabbits on the basis of their calcium and phosphorus metabolism. Blood calcium was reduced in a similar manner in all three groups of rabbits, and wide individual variations in serum phosphorus levels preclude significant deductions. However, the irradiated rabbits suffered disproportionate losses of weight during the fasting period and 4 or 5 of them died during the course of the experiment. The death of these rabbits are attributed to this more rapid consumption of their own tissues and possibly also to suprarenal injury caused both by fasting and by exposure to ultraviolet light.

The Menopause. — Raymond G. Cull. (*Eclec. Med. J.*, **87** : 507, Nov., 1927.)

The climacteric is manifested by menstrual irregularities, dysovarism being its central disorder. The chief symptoms — mental, physical, circulatory and metabolic — involve practically all the endocrine organs, and in proportion as they are related to the ovaries

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Enlargement of the thyroid is possible as a result of climacteric changes but rare. Hypothyroidism is much more usual. Eighty-five per cent of all cases of myxedema occur in women between the ages of 40 and 50. Obesity and metabolic insufficiency occur both in hypothyroidism and the menopause, also constipation. The most uniform of the results of hypothyroidism is cellular infiltration, with its train of symptoms. The estimation of the basal metabolic rate is an accurate measure of the extent of this fundamental change. An almost magical change in which chemical changes are reëstablished follows thyroid therapy. With the unloading of the puffy cells comes a reduction in size and weight of these patients. Marañon believes in an essentially climacteric type of rheumatism as a result of this slowed chemistry. He also states that there is an ovarian type of rheumatism not necessarily at the menopause, and explains that the ovaries require certain stimuli from the thyroid, while the thyroid, having many other tasks, may become functionally played out following acute infections, and consequently its detoxicating function may be defective. Resulting from this infiltration is menorrhagia. Another manifestation of the menopause, which is rare and necessarily a post-climacteric development, is the establishment of the masculine traits. This condition is known as virilism and is probably due to an undue compensatory function of the adrenal cortex.

Treatment is directed along three lines: (1) to lessen the suddenness and extremity of imbalance; (2) to give the organ a longer time and better chance of adapting itself; (3) to endeavor to remove the stress upon the overstrained organs. The last of these is a hygienic recommendation embodying rest, elimination, neutralization, and as suitable an environment as possible. In the second case ovarian therapy is the ideal treatment. In the first case, manifestations of hypothyroidism should be treated with some form of thyroid therapy. Corpus luteum is also given in these conditions. Pluriglandular therapy is often used with great success.

Ovarian Traumatization and Spontaneous Activity.—Ging H. Wang and Alan F. Guttmacher. (*Am. J. Physiol.*, **82** : 335, Oct., 1927.)

It has been shown that it is the secretion from follicular cysts which is responsible for the changes in both the activity of the organism and the structure of the accessory sexual organs found in rats whose ovaries have been moderately traumatized. The only cellular element constantly present in the follicular cysts has been found to be the granulosa layer. Thus, the granulosa cells may have given out the hormone which produced increased activity, cornification in the vaginal epithelium, and hypertrophy of the uterine wall.

Goiter. International Conference. — Berne. F. de Quervain. (*Lancet*, **213** : 1239, Dec. 10, 1927.)

Of special interest for the estimation of thyroid enlargement were the series of preparations set up by the pathological institutes of Freiburg (Aschoff) and Würzburg (B. Schmidt) dealing with the development of the thyroid at various periods of life, and in goitrous and non-goitrous regions. The life-curve of the thyroid, especially brought out by Aschoff, will contribute materially to a clear limitation between normal and morbid processes. If a survey is taken of material derived from various parts of Europe the conviction is soon reached that endemic goiter is fundamentally the same everywhere, and that local differences, apart from the absolute frequency of goiter, are due to relative frequency of the separate forms. In the center of a region where goiter is endemic, the nodular parenchymatous form prevails; at the periphery colloid goiter, diffuse at first, becoming nodular in later life; in the goitrous parts of the lowland separated from the great endemic centers diffuse colloid goiter only exceptionally becoming nodular.

Wegelin discussed the cretin goiter — the most severe form of goitrous thyroid change. The cretin's thyroid is either atrophic with little adenomatous nodules, or there lie in an atrophic matrix nodules of some size, as a rule of a parenchymatous character, in which all forms of secondary changes may occur — calcification, cyst formation, etc. In the cretin colloid is only occasionally formed in a goiter.

Williamson and Pearse drew a sharp distinction between secretion tissue and colloid storage tissue. Should the results of these two investigators be confirmed they would mark the greatest advance of recent years in our knowledge of this subject.

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De Quervain showed that the iodin level in the blood possesses great constancy, and that its height depends on the functional activity of the thyroid gland. It is at its highest in Basedow, at its lowest — only about half or so of the normal height — in the cretin. If the latter is given iodin in excess it is rapidly excreted, since his thyroid gland is not in a position to synthesize it in the normal way. On the other hand, the iodin in the thyroid is partly brought into another chemical combination, whether it is stored up as colloid or whether in this new combination it leaves the thyroid at once without being stored.

Crotti (Columbus, Ohio) found in the blood of goiter-bearers spirilla and protozoa of various kinds, a whole flora or fauna which he thinks he can show also in the water of goitrous neighborhoods. Folley (Paris) related similar independent findings and demonstrated them.

Sexual Indulgence and Growth. — James Rollin Slonaker. (*Am. J. Physiol.*, **82** : 318, Oct., 1927.)

Experiments were carried out with rats as to the effects on growth of varying amounts of sexual indulgence. Females showed greater differences in weight than the males. All groups of females showed a tendency to increase weight after the menopause. Sexual indulgence was associated with an increase in weight in the females and a decrease in amount of follicular hormone. Rats having sexual indulgence showed a tendency to grow more rapidly during early life than abstainers. The bearing of young at an early age appears to have inhibited body growth in later life.

Epinephrin in Progressive Myopia. — Meyer Wiener. (*J. Am. Med. Assn.*, **89** : 594, Aug. 20, 1927.)

The author believes that the stooping posture assumed by myopics for near work causes pressure on the suprarenal glands and has its influence on the progressiveness of the myopia. Properly conducted fresh air exercise brings about an added epinephrin output. Wiener says it seems fair to assume that both exercise and diet influence the secretion of the suprarenals, and that the local application of suprarenal secretion increases tissue metabolism.

Keith thinks that at the root of myopia there must be some fault in the mechanism which normally regulates the growth of the sclera. He asks, "Why cannot it be dysfunction of the suprarenals, or possibly the suprarenals in conjunction with some other gland?

Jean-Henri Dunant

(*Continued from page 17*)

culminated in a meeting in Geneva, in 186[illegible] October 26-29, to which seventeen countries sent representatives and the legal background for the society was drawn up and an insignia chosen: a white band, later embellished by a red cross, virtually the coat of arms of Switzerland reversed. It was worn for the first time in the conflict between Denmark and Germany in 1864, by Dr. Appia, an official of the committee.

Things went well for several years until the failure of Dunant's business in Algiers and Tunis, which necessitated his withdrawal from the Society for voluntary aid. His creditors insidiously criticized him as a "hack writer who was not attending to his business." These assaults against his efforts made Dunant much depressed, so that he withdrew into himself. However, he again attempted welfare work to alleviate the distress of prisoners of war in Paris, but the disturbances in the Commune forced him to give up his efforts. Utterly heartbroken and poverty stricken, he disappeared into England, France and Germany for a long time.

In 1892 Dunant was discovered by the Swiss writer, Baumberger, working in a hospital in Heiden for three francs a day which kept him very modestly. Baumberger told his story in "Ueber Land und Meer" and Dunant again came before the public. The Empress Marie Feodorowna presented him with a pension and when the Nobel Peace Prize was first awarded in 1901, after much discussion and dispute, Dunant received the prize, amounting to about 208,000 francs jointly with Frédéric Passy.

This sudden turn of fortune did not sway Dunant, however, for he went on living in the hospital that had afforded him such pleasant refuge and there he continued his writing in the form of memoirs and articles for the cause of peace. It was his one wish that he be able to personally preside at the Moscow Congress for Peace, and to accept personally his peace award at Stockholm, but, unfortunately, his strength failed and death intercepted his plans on October 30, 1910.

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Parathyroid Preservation. — Wallace I. Terry and H. H. Searls. (*J. Am. Med. Assn.*, 89 : 966, Sept. 17, 1927.)

Millzner, by examination both of specimens removed at operation and of a series of cadavers, found a parathyroid on the anterior capsule of the thyroid gland in 10% and on the lateral capsule in 30% of cases.

Parathyroid Hormone and the Calcification of Fracture Callus. — Edwin P. Lehman and Warren H. Cole. (*J. Am. Med. Assn.*, 89 : 587, Aug. 20, 1927.)

The assumption that, because the injection of parathyroid extract increases the calcium in the blood stream, there will be more available calcium for deposit in fracture callus, is, in the opinion of the authors, a misapprehension that parathyroid extract is of such value. *A priori*, parathyroid extract should not offer aid in hastening or inducing the deposit of calcium in the soft callus about fractures. Its action is to mobilize the fixed calcium in the body. Hunter and Aub, who found that calcium excretion in patients is rapidly increased parallel to an increase in the blood serum calcium on the administration of parathyroid extract say, "The excess of calcium must have come very largely from the bones." The tendency is therefore toward reduction of the calcium in the bones.

The authors undertook a simple series of experiments which tend to support concretely the *a priori* reasoning above outlined. These experiments present evidence showing that favorable results in delayed union that have occurred following the use of parathyroid extract have not resulted from any beneficial action of the hormone. Indeed, if the injection of parathyroid extract has any influence on the rate of calcification of fracture callus, it is that of delaying the process.

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Cardiac Disturbances in Goiter. — John Phillips and J. P. Anderson. (*J. Am. Med. Assn.*, **89** : 1380, Oct. 22, 1927.)

In the study of a large series of cases of diseases of the thyroid gland the frequency with which disturbances of the heart are encountered, particularly in cases of hyperthyroidism is noticeable. These cardiac disturbances vary from a simple tachycardia, or tachycardia associated with various forms of arrhythmia, to cardiac decompensation with engorged liver, ascites and edema of the feet. The occurrence of auricular fibrillation does not appear to bear any relation to the type of goiter that may be present, but rather it appears to depend entirely on the presence and duration of the hyperthyroidism. It is most frequently associated, however, with colloid goiters with adenomatous nodules. Auricular fibrillation is most frequently associated with hyperthyroidism in persons over 45 years of age in whom some degree of arteriosclerosis is already present. Adenomas of the thyroid gland appear to produce cardiac irregularity in some cases before hyperthyroidism has been manifested by an increase in the metabolic rate. In every case of goiter, whether or not hyperthyroidism has been manifested, an examination of the heart should be made to determine the presence of any cardiac irregularity, as it is of the utmost importance that treatment should be instituted before serious heart injury has taken place.

One hundred and twenty cases of auricular fibrillation associated with hyperthyroidism are analyzed. In 75 of the cases in which operation was performed end-results could be obtained, and in 43 of these cases the action of the heart became regular after the removal of one or both lobes of the thyroid gland. The authors feel justified in concluding, therefore, that thyroidectomy is indicated in these cases. If the heart action does not become regular after thyroidectomy, treatment with quinidine may restore the normal rhythm. Even in cases in which the heart action is not restored to a normal rhythm, thyroidectomy will improve the heart action and the rate can be controlled by digitalis. The use of digitalis and of compound solution of iodin for from a week to 10 days prior to operation is advisable.

The Sulfur of Insulin. — Vincent du Vigneaud. (*J. Biol. Chem.*, **75** : 393, Nov. 1927.)

Since evidence has accumulated that insulin is actually a sulfur-containing compound, it becomes imperative to discover the type of sulfur linkage. If the active principle itself actually contains sulfur, as is believed, the evidence presented in this study indicates that this sulfur is present as the disulfide linkage and that insulin is most likely a derivative of cystine. Vigneaud found by means of the phosphotungstic reaction that as the insulin became more purified the cystine content increased. The proportionality was so striking that it gave hope that this might prove to be a suitable means of assay for purified preparations. When the sulfur was split out, the disulfide linkage was destroyed and the test for cystine greatly reduced in intensity, indicating this as the source of the labile sulfur.

Since it has been shown that insulin itself does not give the specific reaction (Sullivan) for cystine, and since the presence of cystine was demonstrated in the hydrolyzed insulin preparations, it must be concluded that the cystine is present as some derivative. Further, the sulfur of the hydrolysate is comparatively stable like free cystine, whereas the sulfur of the original unhydrolyzed insulin is very labile. This change of lability upon hydrolysis is identical with what would be expected of an amino acid derivative of cystine. Glutathione, for example, has a sulfur lability of the order of insulin. Upon acid hydrolysis free cystine would be formed and the sulfur of the hydrolysate would therefore be stable.

The behavior of the sulfur in insulin is quite parallel to the behavior of the sulfur in amino acid derivatives of cystine and suggests that the cystine in insulin is linked to the rest of the molecule by a peptide linkage. In this connection the high arginine, histidine, and tyrosine contents of purified preparations might be recalled.

In Abel's analyses the calculated empirical formula of $C_{45}H_{75}O_{17}N_{11}S$ is based upon the presence of 1 sulfur atom in the molecule. From the author's work on the presence of the disulfide linkage the minimum value would have to be twice that given, or $C_{90}H_{150}O_{34}N_{22}S_2$.

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Hyperthyroidism and the Autonomic System. — Lemoine. (*Presse méd.*, **37** : 440, Apr. 3, 1929.)

M. Lemoine affirms that it is very difficult for clinicians to theorize and explore the vegetative system. He subjected hyperthyroid patients to Danielopolu's atropin test which seems to him to be the best method of sympathetic investigation. Exophthalmic goiter patients were shown to be sympathicotonic according to this test. In order to corroborate this result, M. Lemoine practiced a bilateral cervical sympathicotomy in a hyperthyroid patient. The patient's condition was transformed: fall of metabolism, slowing of the pulse, present tendency to obesity.

Remote and Immediate Results of Treatment of Hyperthyroidism by Short Radiations. — M. Sluys. (*Presse méd.*, **37** : 440, Apr. 3, 1929.)

It seems that the healthy thyroid gland is refractory to the rays. The proof is found in the slight variations of somatic morphology and histology of the gland and respiratory exchanges after very intense expositions of the cervical region for metastases or adenitis. If the rays have an action it is indirect: influence on lymphoid circulation. Very atypical cases and very severe cases should be subject to the rays. Applied with care they no longer give surgical complications. When it is a question of ovarian hyperthyroidism, the results are always good, but more unstable. In all cases medical collaboration is indispensable.

New Classification of Hyperthyroid States; Iodin Treatment of Hyperthyroidism. — Dautrebande. (*Presse méd.*, **37** : 440, Apr. 3, 1929.)

Goiters may be divided into: goiters with normal metabolism (simple goiters of adolescence or colloid goiter, simple adenomatous goiter with degeneration) and into thyroid hypertrophy with increase of metabolism. This latter group includes exophthalmic goiter, severe toxic adenoma, benign toxic adenoma, finally clinically atypical hyperthyroidism. This latter may have two aspects: either that of a simple goiter with raised metabolism, or not presenting any morphologic modification of the thyroid but bearing the characteristics of a nervous tachycardia with raised metabolism. In these two cases, thyroidectomy or ingestion Lugol's solution is effective. A good sign hyperthyroidism is the increase of differen arterial tension (Read and Davies).

Dautrebande's first works on the effica of iodin treatment have received their co firmation by numerous foreign authors. medical therapeusis, iodin will act, provid it is administered continuously, in large do and in fractioned manner.

Insulin in the Treatment of Hyper thyroidism. — Goffin and J. Slosse. (*Pres méd.*, **37** : 440, Apr. 3, 1929.)

The authors administered as much as clinical units to patients in whom the usu treatment had been ineffective. They we able to follow results for two years. In t majority of the cases studied, the auth noted slowing of the pulse, increase in weig and decrease of basal metabolism.

The Most Important Hormonal Di turbances of Childhood and Their Trea ment. — R. Wagner. (*Wien. klin. Wo enschr.*, **41** : 1689, 1928.)

In the hormonal therapy it is importa to determine whether the internal secreti prepared from the gland can replace the fun tion of the gland concerned when introduc into the body. Up to the present, three su internal secretions are available: thyrox parathormone and insulin. Adrenalin a pituitary have, to be sure, a marked pharm colcgico-dynamic activity, but are not to considered as bearers of a substitution the apy. Thyroid treatment is of greatest imp tance practically. Thyroxin as well as t oral administration of desiccated thyr comes into consideration here as comple substitution therapy. Pituitrin is an excelle symptomaticum for definite forms of diabe insipidus, but must be injected 1 to 2 tim daily, continuously, like insulin.

Contribution to the Organotherapy Obesity. — H. Ueberall. (*Med. Klin.*, 1839, 1929.)

Although thyroid preparations are to named as remedy of choice in endogen obesity, there are forms of obesity wh although conditioned endogenously, do n respond to thyroid medication or make impossible through pathological reaction.

The circumstance that pure, monoglandu forms of obesity probably do not occur and

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attempt at polyvalent treatment, led to the preparation of pluriglandular reducing agents. These preparations are to be preferred to pure thyroid medication; still they contain thyroid in addition to other substances. For cases which are sensitive to thyroid medication there are also thyroid-free pluriglandular preparations.

The therapy is tolerated without untoward symptoms. Increases in basal metabolism and decrease in weight give evidence of the activity of the medication, even when used for a long period of time without reduction of diet, which is itself by no means inferior to thyroid medication.

Prognosis and Therapy of Intermittent Claudication and of Incipient Gangrene of the Extremities. — H. Schlesinger. (*Med. Klin.*, **25** : 18, 1929.)

The idea certainly is strongly suggested of causing a marked vaso-dilatation through organotherapeutic measures. The author repeatedly used a preparation prepared from normal vessel walls (albumin-free), which was given intravenously 1 to 2 injections a week in doses of 5 to 10 cc. According to the experiences up to the present the measure seems to exert a favorable action on the disease process, but is apparently not superior to the nitrites.

Owing to the preponderance of the disease in the male sex, it can be assumed that the female sex glands exert a protective influence on the vessel wall; proceeding from these considerations the author repeatedly attempted the treatment of this disease with ovarian preparations, in men. Concerning the results of this method of treatment, which are not yet settled, the author will make a report later.

Concerning the Point of Attack of Insulin. — Bürger and Kramer. (*Münch. med. Wochenschr.*, **76** : 178, 1929.)

Experiments of the author show with certainty the fact that the action of insulin on carbohydrate metabolism is united to the co-operation of the musculature. In the first 20 to 40 minutes after the intravenous injection of insulin there regularly occurs in man and in dogs an increase in blood sugar (primary paradoxical insulin hyperglycemia) which remains absent when the liver is removed from the circulation and on the other hand becomes maximum following the injection of 2 units per kilogram dog into the trunk portal vein.

Concerning Capillary Microscopy in Children. — Doxiades. (*Verein inn. Med. u. Kinderheilk., Berlin*; Session of Jan. 28, 1929.)

In fainting fits the visible capillaries become empty. Adrenalin increases the amount of circulating blood. If thyroxin is administered for a long time, the capillary picture frequently becomes normal.

The Early Diagnosis of Pregnancy from the Urine Through Administration of the Pituitary Anterior Lobe Hormone (Zondek-Aschheim Reaction). — Ehrhardt. (*Münch. med. Wochenschr.*, **76** : 82, 1929.)

The author tested the Zondek-Aschheim reaction in 197 cases and obtained correct results in 194 cases. In the preponderant majority of cases the diagnosis could be determined macroscopically.

Concerning Treatment of Female Sterility. — K. Amersbach. (*Münch. med. Wochenschr.*, **76** : 15, 1929.)

The author reports concerning a case in which the serologic test showed marked hypofunction of the pituitary and ovary. Accordingly, a corresponding etiologic therapy was given: namely, organotherapy with anterior pituitary preparation combined with ovarian preparations, at the same time diathermy and light stimulative radiation of the ovaries. The result of this treatment was at first regulation of the menses, later actual pregnancy. In another case in which sterility appeared in amenorrhea due to hypofunction of the ovaries, in hypofunction of the thyroid and later adiposity and growth of hair on the cheeks, thyroxin, an ovarian preparation, diathermy and balneotherapy were prescribed. Result: loss of 14 pounds in weight, appearance of slight menstruation once. Up to the present time no pregnancy; growth of hair on the cheeks uninfluenced.

Treatment of Diabetes with Pneumothorax and Insulin. — L. M. Blum. (*Paris méd.*, **19** : X, 92, 1929.)

In addition to cases in which insulin treatment undoubtedly has a favorable action, some also come under observation in which insulin effects a more rapid development of

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pulmonary processes. Nevertheless insulin therapy is always to be tried and when possible to be combined with application of a pneumothorax.

Concerning Insulin-Forced Alimentation. — Fellegi. (*Med. Klin.*, **25** : 263, 1929.)

Since opinions concerning insulin-forced alimentation are still divided, the viewpoints coming into consideration should be discussed. (1) The foundation of a successful treatment is the administration of proper doses. Small doses of insulin give results only when it is a question of quite healthy persons, who despite good appetite are unable to take on weight. (2) Insulin is to be given in increasing dosage. (3) The result of treatment depends on the course of the hypoglycemic reaction. The prescription of the exact time of food intake is not correct, since the appearance of the hypoglycemic reaction depends not only on the size of the dose but also on the sensitiveness of the patient to insulin. (4) The meals should not begin with the eating of carbohydrate. (5) Immediately before injection nothing should be eaten. (6) Glucose should not be injected at the same time as the insulin. (7) Insulin is indicated only when the gastrointestinal tract is free from organic changes. (8) The increase in weight obtained during the insulin treatment continues even after termination of the treatment. (9) In patients with pronounced dyspeptic complaints, good results are obtained when a pancreas preparation is prescribed at the same time as the insulin. (10) According to the author's experiences insulin is not contraindicated in chronic, fibrous and fibrocavernous forms which show merely moderate rise in temperature and mostly a slow course. In the insulin treatment of tuberculosis, the prevention of a possible hypoglycemic reaction is especially important.

The Action of Pepsin on Insulin and Its Acetyl Derivative. IV. Contribution concerning Insulin.—W. Dirscherl. (*Hoppe-Seylers Zeitschr. physiol. Chem.*, **180** : 217, 1929.)

In extensive measurements Dirscherl found that the action of pepsin on insulin is irreversible and may not be made to retrograde. The author agrees in this with the findings of A. Harteneck and W. Schuler.

Further experiments show that the action of pepsin on insulin fits into the category of a ferment action; in particular the dependence on time and temperature does not favor the opinion that the inactivation of insulin can be occasioned by an absorption of pepsin. It can be admitted especially that the inactivation of insulin through pepsin rests on a decomposition of albumin. If insulin itself is an albumin substance, it must be of that complicated type which is affected by pepsin. In the treatment of suspended acetyl insulin with pepsin, the influence is very limited.

Formaldehyde inactivates insulin in pH 7 in a moderate time reaction. The preparation may be precipitated and is again brought to an activity of about 25 per cent of the original insulin by heating with N/10 hydrochloric acid. In this treatment with acid in heat the active portion is precipitated. Insulin itself behaves quite similarly in the presence of hydrochloric acid in heat. Blatherwick and his associates also found insoluble insulin fractions.

Anemia in Rats and Liver Treatment. — A. Orban. (*Monatschr. Kinderhlk.*, 42 : 402, 1929.)

The following conclusions are to be drawn from the rat experiments undertaken. (1) Liver feeding does not have an accelerating action on the blood regeneration in rats who have been rendered anemic through withdrawal of blood, even when liver extract or liver residue is given. (2) Feeding of liver is unable to accomplish a vitamin effect under the experimental conditions prepared by Orban. (3) Since an accelerating action on blood regeneration did not appear in the experiments mentioned, the action of liver does not appear to be a simple stimulus to regeneration.

Concerning the Influence of Atropin, Adrenalin and Amyl Nitrite on the Size of the Heart. — D. Scherf and E. Zdansky. (*Wien. klin. Wochenschr.*, **42** : 60, 1929.)

Following intravenous injection of 0.05 cc. of 1 per cent solution of adrenalin an enlargement of the heart was never observed in individuals with normal heart and blood vessels, but in a part of the cases a distinct diminution could be deduced from the kymographic curves. An enlargement was not observed when the blood pressure rose over

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200 mm. mercury. This is explained by the fact that the heart reducing, positive inotropic action and the acceleration of frequency were equal to or even surpassed the heart enlarging action of the rise in blood pressure. In several cases in addition to the diminution of cardiac caliber, a diminution of the size of excursion of the cardiac rims was present which may be in all probability concluded to be a decrease of cardiac output.

Modern Treatment of Skin, Urinary and Sex Diseases.— H. Colman. (*Med. Klin.*, **25** : 192, 1929.)

In acne vulgaris in addition to other preparations and purgatives an organotherapeutic treatment with preparations such as lutein, thyronucleoprotein, adrenucleoprotein is to be used as internal medication.

Therapy of Paroxysmal Tachycardia and of Extrasystole. — E. Maliwa. (*Mitt. Volksgesdhtsamies*, **1** : 23, 1929.)

In many cases it is sufficient to use quinine and quinidin. There are, however, cases refractory to quinine. In such cases it is recommended that 1 cc. adrenalin in 10 cc. physiological salt solution be injected intravenously.

Treatment of Adiposity. — H. Erdman. (*Die med. Welt*, **3** : 169, 1929.)

Among the therapeutic measures endocrine preparations are also to be mentioned, especially the thyroid hormone which furthers metabolism. Thyroid preparations can also be of assistance in obesity due to over-eating, but they have a great disadvantage: they have a harmful effect on the heart.

The Thyroid Problem. — Walter M. Boothby. (*Endokrinologie*, **3** : 1, 1929.)

Thyroxin is a catalyzer which accelerates the production of heat by increasing the basal metabolism. It is of importance practically that the curve of the fall of the thyroxin action takes its course according to definite mathematical rules. The action of thyroxin on growth and physical and psychic characters is to be considered as secondary. The treatment of myxedema is to be directed towards two goals: (1) elevation of the production of heat through increase of thyroxin concentration in the tissues to the normal value and maintenance at the normal value. Accordingly the dosage should be sufficiently large in the first week, that a decided surplus is present. The treatment should be a lasting one and not intermittent and the amount of thyroxin given daily following the initial period should be exactly the amount of that destroyed daily. The amount of thyroid preparation required is of course dependent on its thyroxin content; since the normal amount of thyroxin in the body is somewhat less than 14 mg. This amount must accordingly be given. With regard to endemic cretinism it must be said that possibly a limited number of cretin cases (hypodysthyrosis of de Quervain) may be treated successfully if iodin were combined with desiccated thyroid.

The Eye in General Medicine. — A. Patry. (*Rev. méd. Suisse Rom.*, **49** : 29, 1929.)

Hypertrophy of the endocrine glands calls forth eye disturbances of mechanical nature. To this group belong the manifestations of exophthalmic goiter, conjunctival congestion, recurring hemorrhages of the vitreous humor in juvenile hyperthyroidism, the retinal spasms through disturbances of equilibrium of the thyroid or ovary. Baillart found spasmodic crises in a case of dysmenorrhea. Administration of thyroidin changes the ocular pressure. Muller effected distinct improvement in three cases of glaucoma through pituitrin. Trophic disorders, blue sclera, brittleness of bone are to be attributed to polyglandular etiology and hypoglycemia or dysfunction of the parathyroids. We are familiar with forms of cataract due to genital, parathyroid and thyroid disturbances. Endocrine cataract belongs in the range of internal secretory disorders. It develops during pregnancy as well as at the time of involution of the sex glands. The cataract of old people is to be attributed to a profound disturbance of the endocrine glands. Sigrist was able to extract a hormonal substance from the parathyroids with which he treated cataract cases with some success. Diabetes promotes and at least accelerates the appearance of "senile cataract."

Therapeutic Attempt in Urticaria. Allergic Diet. — Teran Argüelles. (*Zentr. ges. Kinderheilk.*, **22** : 676, 1929.)

After various investigators had made the observation that spleen extract suppresses

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eosinophilia, pruritus, asthma and other allergic diseases or at least assuages them, the author attempted to treat severe cases of urticaria in children with spleen extract. The extract was administered before meals and influenced cases favorably which had remained refractory to every other therapy.

The Cholecystographic Test of Motility of the Gall Bladder and Its Results. — H. Bronner. (*Fortschr. Geb. Röntgenstr.*, **39** : 23, 1929.) (The Test of Evacuation by Means of Pituitrin Injection, page 29.)

The introduction of pituitary preparations used by Kalk and Schöndube as measure for the determination of the gall-bladder content, possesses extraordinary certainty of action according to several publications of these authors and also of other authors. Several exceptions to the action were also determined; the degree of evacuation of the gall bladder obtained was, however, subject to strong variations. If a whole series of authors have frequently observed only a partial evacuation, this circumstance doubtless serves to lessen the usefulness of the method for clinical cholecystography. It is important to stress in this connection that several authors could determine a decided cholekinetic superiority of physiological food stimulus as opposed to pituitary preparations in comparative investigations and Bergmann noted: among the cholekinetics, pituitrin is only one, and not the strongest. As the strongest agent to obtain the condensed cystic bile, the emulsion of egg yolk in oil may be considered. Bronner also believes that the pure yolk meal is to be recommended as the useful and reliable normal procedure for the clinic.

Hyperglycemia and Senile Cataract. — J. Galindo. (*Med. Ibera*, **24** : 482, Apr. 13, 1929.)

Recent studies of Marañón and other authors have shown the presence of symptoms and complications of diabetes in patients without glycosuria, but with spontaneous or induced hyperglycemia. The author systematically investigated the blood sugar curve in his cases of cataract and found that 58.5 per cent of the cases were either plainly diabetic or presented curves of prediabetic hyperglycemia. It was not possible to determine in these cases whether it was a question of actual diabetic cataract or of senile cataract coincident with the diabetes. Although the genesis of diabetes is very obscure it is evide that its production is related to metabo disturbances, principally of diabetic type. the author's opinion, an analogous pathoge esis should be invoked to explain glaucom From the practical viewpoint, the knowled of these cases is normally important. T oculist is accustomed to analyze the urine a not to operate without a preliminary trea ment of the diabetic patients. If there is sugar in the urine, however, he considers the to be healthy when it may be a question latent hyperglycemia. Another interestin aspect of the question is the possibility treating cataract medically. Joslin has alread pointed out the interesting fact that th opacity of the lenses in incipient diabet cataract decreases with the general trea ment and with the improvement in th diabetes. It seems to be a certain fact tha cataract is related to hyperglycemia by th frequency with which it is present in youn diabetics who have suffered the disease fo many years. On the other hand the signifi cant fact of having found 58.5 per cent cataracts in hyperglycemia coincides with th opinion of Marañón and the observation two patients with incipient cataracts wh have been subject to adequate diet sinc October, and who at the present time hav their cataracts arrested and preserve the sam vision, inclines the author to think of th possibility of a medical treatment of cataract In order to do this, an early diagnosis cataract is of great importance. For this pur pose, the corneal microscope and the sli lamp are very useful. Once this early diag nosis has been made and in case this is positiv and shows an alteration of carbohydra metabolism medical treatment of the cata ract should be undertaken with diet and sma doses of insulin.

The author's opinion concerning the tim for operation of diabetic cataract is this before operating the cataract an analysis blood sugar should be made to determine th curve of glycemia. With respect to the con dition in which a diabetic should be in orde to be operated upon, he agrees with the wor of Marañón and Blanco Soler that diabeti patients in order to be operated upon shoul be without glycosuria and with normal bloo sugar, during the operation as well as post operatively.

In the discussion, Dr. Nogueras stated tha he had seen some cases of cataract wit

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hyperglycemia but without glycosuria. In incipient cataracts he had observed improvement produced by insulin, including a case with normal blood sugar curve.

Investigation concerning the Influence of Various Altitudes on the Action of Thyroid in the Dog. Contribution III. — R. E. Mark. (*Naunyn-Schmiedebergs Arch. exp. Pathol. u. Pharmakol.*, **139** : 68, 1929.)

The action of various diets on hyperthyroidization at an altitude of 2000 m. was investigated. It was found that slight undernutrition of dogs with carbohydrate as well as meat diet is tolerated with less loss of weight at an altitude of 2000 m. than on the plane level. Definite nitrogen retention exists at this level. The water requirement was greater with the same diet at this level than in the later experiments on the plane level. In dogs which in preliminary experiments on the plane had shown complete hyperthyroidization, essentially weaker thyroid action appeared at the higher level. In animals again brought to the plane an after-effect of the higher level existed for about 3 weeks. Hyperthyroidization was of course far inferior to the action of the thyroid doses in the preliminary experiment.

Blood Sugar Investigations in Diabetics Treated with Insulin. — N. A. Nielsen. (*Zeitschr. klin. Med.*, **109** : 637, 1929.)

The blood sugar was tested every hour for 24 hours in 8 diabetics under insulin treatment. It was shown that the test of the morning blood sugar alone did not give a clear picture of the action of insulin on diabetic hyperglycemia, in any of the patients. The value, measured 5 hours after insulin in all these patients, lies at a more or less pronounced level of the curve, at its minimum or close to it. This is the case following the injection in the morning, after the injection at night and also when the dose is changed. This value accordingly gives a far better picture for the action of insulin on the blood sugar. Through determination of the blood sugar before and 5 hours after the injection of insulin we obtain a good idea of the appearance of the 24 hour curve, since this takes its course equally rising or falling between two values. If two injections are given, the best picture is obtained through determination before and 5 hours after each injection. From the curves it is shown that under insulin treatment, sugar analyses must be undertaken on portions of the urine, which are excreted shortly before the injection of insulin, since the blood sugar is highest here. Moreover, it is recommended that a portion of the urine which has been excreted several hours before the morning injection be examined in severe cases, since this portion will certainly be free from sugar, owing to the late and steep rise in blood sugar in some cases. The behavior of the curve corresponds to the clinical estimation of the severity of the case, since in more moderate forms of the disease curves with slighter oscillations are found and in more severe forms of the disease, curves with greater oscillations occur.

Concerning Bronchial Asthma. — M. Matthes. (*Wien. med. Wochenschr.*, **79** : 214, 1929.)

The acute attack of asthma must, to be sure, be controlled as actively as possible. Adrenalin is the most effective in the majority of cases. In general this therapy is harmless even though we do occasionally find individuals who respond to the injection with violent cardiac activity. That continued use of adrenalin leads to obesity as Lorand maintains, the author has never observed. Outside of adrenalin the author also uses ephedrin and synthetic ephedrin, antipyrin and caffein.

Revivification Experiment on Desiccated Animal and Human Organs. — Morosow. (*Die med. Welt*, **3** : 153, 1929.)

The author studied the action of various pharmacologic preparations on the blood vessels of the mummified rabbit ear. The drugs used were adrenalin, nicotin, cocain and caffein. Caffein exerted no action on the ear vessels, although it was introduced in high concentration. All the vaso-constrictor preparations exerted their characteristic action on the blood vessels, but in a slighter degree than normal. Thus, for example, the vessel lumen contracted not more than about 68 per cent upon the introduction of 1 cc. adrenalin in a solution of 1:1000, whereas a similar dose into the vessels of normal organs occasions complete and exceedingly long continued spasm. Isolated frog heart which has been desiccated to 25 per cent loss of weight and flushed with Ringer's solution showed contractions which, though weaker than normal, continued for many hours and were increased

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in their frequency and intensity by the addition of L. Haberlandt's hormone of heart motion. The author believes that the experiments which were also undertaken on hearts of human embryos, suggest a hitherto not accepted property of the tissues of vertebrates and outside of their general biological significance they also have a positive interest for the practicing physician.

Pituitary Dwarfism. — H. Lucke. (*Zeitschr. Konstitutionslehre*, **14** : 430, 1929.)

Report concerning a case in which, through successful organotherapy, evidence of pure pituitary disorder (diagnosed from the clinical picture) was obtained. It was even found that these diseases may be influenced to such an extent through substitution treatment of sufficient duration that these often psychically normal dwarfs can take up the struggle for existence like other normally grown individuals through the possibility of approximation of their physical form to the normal. In the author's case it was a question of a 12½ year old girl (4 years ago), who was born normal, but remained backward in physical growth for several years. On the basis of established findings a disease of the pituitary was assumed — an insufficiency of the anterior lobe. Recourse was had to organotherapy and treatment with pituitary anterior lobe introduced. The child first received one injection daily, later three, and then 2 tablets daily. The child is now 15 years old, still somewhat small, but certainly not to be described as a dwarf. She grew about 28 cm. within 1½ years. The anomalies of metabolism have also adjusted themselves extensively.

Unusually Large Thyroid Dosage. Its Dangers: Case Report. — L. E. Parkins. (*New England J. Med.*, **200** : 231, 1929.)

Report concerning a patient who in a period of time of 4 years took 667.3 gm., accordingly an average daily dose of 0.53 gm. thyroid extract. The patient had dyspnea, severe cyanosis, pulmonary edema and great amounts of blood tinged sputum. Thyroid medication was of course immediately discontinued and morphine and bromide given. After 10 days the patient had recovered and was dismissed able-bodied. The author draws the conclusion that thyroid extract treatment in obesity should not be undertaken without determination of the basal metabolism, that, moreover, a long continued use of the remedy in large doses can cause tachycardia, dyspnea and acute pulmonary edema, that the remedy does not act locally in the usual doses.

A Case of Cryptogenetic Pernicious Anemia Resistant to Simple or Mixed Liver Treatment. — P. Émile-Weil. (*Presse méd.*, **37** : 521, Apr. 20, 1929.)

The author reports a case of cryptogenetic pernicious anemia diagnosed clinically and corroborated by necropsic examination, which proved to be resistant to liver treatment, as well as to transfusions completed by insulin therapy. Then within 1 month he obtained an important improvement (gain of 9 pounds, rise of blood cell count from 1,000,000 to 2,700,000, fall of globular value from 2 to 1) by combining the various methods. The patient left the hospital for the country but returned at the end of 6 weeks with recurrence and the treatment which had been effective before the recurrence, no longer gave any result. Death occurred at the end of 2 months with the blood in a state of panmyelophthisis.

On the subject of this case the author speaks of cases of Biermer's disease which proved resistant to liver.

In the discussion, N. Fiessinger stated that he had also observed failures with Whipple's method in pernicious anemia. One case in particular in which the blood formula had returned to normal at the end of a month's treatment with liver, presented new signs of pernicious anemia 4 months after cessation of the treatment. This time the disease was not modified by liver nor by liver extracts. In two other cases in which it was a question of aplastic pernicious anemia, he was unable to obtain results with Whipple's method. It would seem that the Americans have especially treated cases of plastic pernicious anemia; it is in these forms that the reaction of the red blood cell picture which they describe, is observed.

M. Tixier reports failures of Whipple's method, in cases of pernicious anemia of childhood especially, which appear to be more difficult to treat than that in adults. It is possible that the extracts of liver act like insulin in diabetes, Biermer's disease continuing to exist.

P. Émile-Weil draws attention to the fact that in his case the anemia was not entirely aplastic. Liver extracts are useful but have not the same value as liver in nature.

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M. Monier-Vinard stated that even though he had obtained marvelous results with Whipple's method in pernicious anemia, he had noted its ineffectiveness in another form of severe anemia, the anemia of benzine poisoning where he observed no sign of restoration of the blood picture. In these cases there is a considerable diminution of polynuclears which persists despite liver treatment and perhaps the prognosis might turn to profit the comparison of the variations of the leucocyte formula.

P. Émile-Weil stated that he was also unable to influence benzolic anemia and anemia due to thorium by liver treatment. In several cases of severe anemia due to arsenobenzol he noted that the first improvement is a modification of the leucocyte formula. No characteristic permits one to separate these different anemias or to know whether the medicine will act.

M. Chevallier distinguishes two entirely different groups of affections. Pernicious anemia on the one hand and hemorrhagic aleukemia on the other, the latter being characterized by a marked anemia with considerable diminution of white cells and especially of polynuclears, hemorrhages and an absolute resistance to all types of therapy. The prognosis of the severe anemias is governed in his opinion by the modifications of the white cells.

Basic Properties of the General Regeneration Hormone. — R. Fraenkel. (*Arch. klin. Chir.*, **154** : 398, 1929.)

In experiments which were performed independently of the works of Lorin-Epstein, the author found that in warm blooded animals and also in human beings the course of regeneration is guided by furthering and inhibiting substances in the blood: a substance which kindles the growth of the regeneration but in general inhibits the differentiation and another substance which accelerates differentiation, hence inhibits growth. The plastic hormone can not be identical with the decomposition substance absorbed. Since its action increases exactly parallel with its amount, it may be assumed that the absorption of decomposition substance causes a formation or appearance of the plastic hormone. The possibility also exists that this arises secondarily from the decomposition substance. The site of formation or transformation is unknown.

Lorin-Epstein considers the differentiation hormone as an antibody against the decomposition substance. This conception can not be correct. A further difficulty rose with the knowledge that decomposition substance and plastic hormone are not identical; for in this way the direct relation of the differentiation hormone (first appearing later) with the decomposition substance becomes especially doubtful. It is conceivable that the differentiation hormone is directly transformed from the plastic hormone. In any case it is shown that to an increased formation of the plastic hormone there corresponds, later, an increased action of the differentiation hormone. The guiding substances acting on the regeneration processes (following injuries) from the blood correspond to the definition of functional nature which Asher has given for hormones. They should accordingly be correctly designated as plastic and as differentiation hormone.

The actions of both hormones depend on the "disposition" of the regenerating tissue.

Concerning the Effects of Liver Therapy in a Severe Post-Hemorrhagic Anemia in an Azotemic. — Labbé, Boulin, L. Justin and Gouven. (*Presse méd.*, **37** : 209, 1929.)

Report concerning the course of the illness and the results of treatment in a patient who suffered from chronic azotemic nephritis and showed symptoms of severe anemia following metrorrhagia caused by a fibroma. Under the influence of a liver treatment (administration of liver extract) the regeneration of the constituents of the blood set in very rapidly. The red blood cell count tripled within a period of 14 weeks, although the existing azotemia showed an essential increase.

Concerning the "Hormone" of Spontaneous Uterine Contractions. — J. Voegel and N. Margolina. (*Arch. Gynäkol.*, **135** : 478, 1929.)

The study of the spontaneous contractions of the smooth musculature is considered at the present time from the new "hormonal" standpoint. Le Heux cleared up the properties of cholin — of the "hormone" of the intestinal wall; it is secreted in the contractions of the intestinal wall and is able to induce movements of the intestinal musculature and to strengthen them. The "hor-

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mone" of heart motion has specific action according to the opinion of Demoor and Haberlandt and possesses specific properties of the known hormones. The authors obtained the following results with regard to the uterus in their experiments: an isolated uterus (rabbit's) cornu which had remained in Ringer-Lock's solution (R-L) with continuous current of air or O_2 administration, after normal, automatic, rhythmic contractions of 10 to 12 minutes, begins to give stronger and more frequent contractions which at times assume a tetanic character (asphyxia of the isolated piece). If the Ringer-Lock solution in which the isolated piece of uterus had been is replaced by pure Ringer-Lock solution, the tetanic character of the contractions disappears and the latter again become rhythmic.

The isolated piece of uterus gave the same regular rhythmic contractions in flowing Ringer-Lock solution for hours. The R-L solution in which an actively contracting rabbit uterus had been present for 2 to 3 hours, stimulates the contractions of this isolated organ. The Ringer-uterus solution possesses no individual specificity. Its chemical investigation reveals: (1) a decrease of alkalin reaction, (2) a decrease of the glucose content and (3) a rise of the calcium content in comparison with pure and flowing R-L solution in those cases where it had exerted a contraction-stimulating action.

Pancreatic Function. IV. The Humoroneural Regulation of the Gastric, Pancreatic and Biliary Secretions. — S. Okada, K. Kuramochi, T. Tsukahara and T. Ooinoue. (*Arch. Int. Med.*, **43** : 446, Apr., 1929.)

In general, epinephrin inhibits the secretion of digestive juices and insulin accelerates it. The mechanism of this inhibitory and excitatory action, however, is unknown. The purpose of this study was to solve the *modus operandi* of the regulatory mechanism of the secretion of the digestive juices, so necessary for the welfare of man and animals.

The authors found that:

1. Insulin provokes gastric, pancreatic and biliary secretion, and epinephrin inhibits it (only the influence of epinephrin on the gastric secretion is not so decisive). Ephedrin has an effect similar to that of epinephrin. The increased secretion of these juices after the injection of insulin is marked in the presence of a pronounced hypoglycemia, while it is nearly negative in the absence of hypoglycemia. The decrease of the secretion of the juices after the injection of epinephrin go parallel with hyperglycemia, and is followed by an increase of secretion when a reactive hypoglycemia occurs.

2. Also in cases of cancer of the stomach in which the gastric juice remained alkalin during the course of the collection, a marked increase of the secretion of pancreatic and biliary juices after the injection of insulin was observed, indicating that insulin primarily stimulates the secretion of these juices.

3. The increased secretion of gastric and pancreatic juices and of bile induced by the injection of insulin is almost completely inhibited by an injection of dextrose, but a profuse secretion again occurs when hypoglycemia recurs. Therefore, it is definitely shown that hypoglycemia, if it does not also stimulate the secretion of these juices, does so when insulin is injected.

4. An injection of atropin causes a distinct inhibition of the increased secretion of these juices induced by the injection of insulin, indicating that hypoglycemia exerts its stimulating effect on the centrum of the secretory nerve and that the stimulus is transmitted to the acting tissue cells through the parasympathetic nervous system.

5. When dextrose is introduced into the duodenum, it usually brings about an initial increase of the secretion of pancreatic juice and of bile, perhaps as a reflex evacuation of the gall and pancreatic tracts, including the gall bladder. Hyperglycemia, after resorption of the dextrose, however, stops the secretion of pancreatic and biliary juices almost entirely, and the gastric content becomes achlorhydric. Following the hyperglycemia, a reactive hypoglycemia is evoked which is accompanied by a profuse secretion of digestive juices. An intravenous injection of dextrose has almost the same effect, except that the initial increase usually does not occur and the diminution of the gastric secretion is manifested in amount rather than in acidity. An isotonic or rather a somewhat hypotonic solution of dextrose has the same inhibitory influence on the secretion of the digestive juices as a hypertonic solution, if the amount is sufficient. Therefore, it is definitely proved that hypoglycemia, in general, stimulates the secretory nervous centrum and hyperglycemia inhibits it and that the

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stimulus is transmitted through the parasympathetic nervous system to the reacting tissue cells, while the inhibitory impulse most likely is transmitted through the sympathetic nervous system.

6. The test breakfast does not cause any secretion of acid or cause a markedly diminished secretion of acid by the stomach at the stage of hyperglycemia, in comparison with its effect on the secretion of acid at a time of fasting. The motility of the stomach is also inhibited, so that the bread remnants of the test meal are detectable for a much longer time by fractional suction. Hypoglycemia is accompanied usually by hunger and hyperglycemia by a "full feeling."

7. Since hypoglycemia induces a humorally excitatory impulse and hyperglycemia an inhibitory impulse to the secretory centrum and since from this centrum the stimulus and the inhibitory impulse are transmitted through the autonomic nervous system to the acting tissue cells, this process might be called the "humoroneural regulation of the secretion of the digestive juices." The secretion of saliva is excepted from this regulation.

8. In diabetes mellitus, the same inhibitory and excitatory mechanism is also in force, being different from that in normal cases only in the manner of entrance of these impulses. It is evident from this fact that it is the process of the alternation of hypoglycemia and hyperglycemia that stimulates the excitatory and the inhibitory functions of the secretory centrum and not the durable state of them, which perhaps causes an accommodation such that stimulation is not any longer induced.

9. The humoroneural regulation and the humoral mechanism normally cooperate without interference with each other, an intravenous injection of secretin causing nearly as abundant a secretion of pancreatic juice at the stage of hyperglycemia as at a time of fasting. When hyperglycemia develops, gastric secretion ceases and the entrance of the acid chyme into the duodenum also ceases, so that the secretin mechanism does not have any occasion to function during this period. A hypoglycemia causes a profuse secretion of gastric juice and an abundant gush of acid chyme into the duodenum, which, in turn, induces the full functioning of the secretin mechanism. When, however, a disturbance of gastric secretion occurs, as in achylia gastrica and in cancer of the stomach, the humoroneural regulation alone, without the cooperation of the secretin mechanism, excites the secretory glands of the pancreas to activity.

10. Histamin, a vigorous excitant of the gastric secretion humorally, causes also a profuse secretion of gastric juice at the high point of hyperglycemia. Therefore, it follows that the humoroneural regulation does not have any remarkable influence on the humoral mechanism and this, in turn, proves that the action of histamin does not have anything to do with the neural mechanism.

Concerning the Action of Pancreatic Extracts on Arterial Pressure. — Gley and Kisthinios. (*Paris méd.*, 19 : XI, 93, 1929.)

The authors have shown that a substance can be extracted from the pancreas other than insulin which is positively to be distinguished from insulin and possesses the property of lowering arterial pressure which is demonstrable clinically as well as experimentally. The authors stress the priority of their observation in comparison with other authors.

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A Record of Progress in the Study of the Internal Secretions and Metabolism

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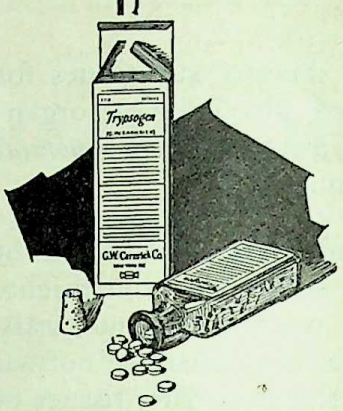
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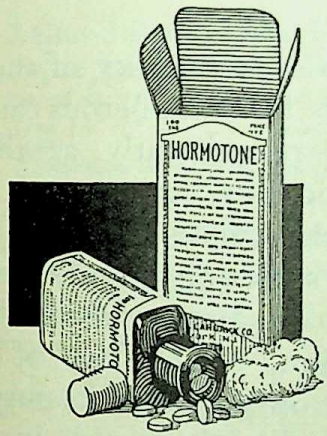
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"It is thus seen that the existence of a definite relationship between the anterior pituitary gland and the female pelvic organs has been established." (C. F. Fluhmann, *Am. J. Obstet. and Gynecol.*, 1929, XVIII, 745.)

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Exophthalmic Goiter

A DISTINCTION is frequently made between "true" exophthalmic goiter and toxic adenoma. This distinction is here discussed.

(CONTINUED FROM VOL. XIII, No. 6)

In preceding articles we have reviewed the current views on etiology and pathogenesis. Four major theories of the latter were discussed — thyreogenic (including dysthyroidism), neurogenic, constitutional hyperreactivity and thymic constitution. This article deals with the condition now usually described as toxic adenoma of the thyroid and its relation to exophthalmic goiter. In a recent article[1] Ginsburg reviews the work of the several observers who have described this syndrome and gives the following list of authors and the names under which they describe it.

"Enlargement of the thyroid gland in connection with enlargement or palpitation of the heart — Parry (1825).

"Constitutional iodism — Rilliet (1859).

"Iodine exophthalmic goiter; iodine Graves' disease — Trousseau (1860).

"Formes frustes exophthalmic goiter — Trousseau (1862); Marie (1883).

"Secondary Basedow — Gautier (1893); Buschan (1894).

"Basedowified goiter — Marie (1897); Struma basedowificata — Kocher (1906).

"Goiter heart — Kraus (1898).

"Iodine thyroidism — Breuer (1900).

"Basedowid — Stern (1908-1909).

"Toxic nonexophthalmic goiter — Plummer (1912).

"Toxic adenoma of the thyroid — Plummer (1913).

"Adenoma with hyperthyroidism — Plummer (1916).

"Hyperfunctioning adenomatous goiter — Plummer (1921).

"Iodine hyperthyroidism — Jackson (1924).

"Nodular goiter with hyperthyroidism — Rienhoff (1927)."

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In recent years the name of H. S. Plummer has become more closely associated with the conditions than any other. In numerous publications he has set forth his views, distinguishing toxic adenoma as a condition apart from exophthalmic goiter. "In terms in common use in American literature, the best grasp of the subject can be obtained by classifying goiters as endemic and exophthalmic. The endemic goiters may be divided into the diffuse colloid and the adenomatous; and the adenomatous into those with and those without hyperfunction . . ."[2].

"ENDEMIC GOITER. — A supply of iodin adequate for the proper functioning of the thyroid, followed by a subnormal delivery of thyroxin to the tissues, produces hypothyroidism; consequent elevation of intensity of thyroid stimulation causes diffuse hypertrophy of the thyroid; the secretory processes are altered; the diffuse hypertrophy disappears; colloid is stored in excess of the normal, and diffuse colloid goiter is the result. In many cases the sustained stimulation of the thyroid, in conjunction with unknown factors, causes the development of new tissue, adenomatous goiter. Relatively late in the life history thyroids containing this tissue in many instances hyperfunction, and the entity hyperfunctioning adenomatous thyroid appears.

"EXOPHTHALMIC GOITER. — Intensive stimulation, of unknown origin, of the entire functionally capable and probably primarily normal thyroid causes diffuse hypertrophy; an abnormal amount of thyroxin and an abnormal thyroid product is delivered; during periods of remission of intensity of stimulation and an adequate iodin supply, the diffuse hypertrophy disappears in some instances and colloid above the normal amount is stored. Under the stimulation, acini which are possibly more or less new, as a rule, develop. In exceptional cases the gland, particularly after a portion has been resected, becomes much larger from the development of new tissue. This should be sharply distinguished from the adenomatous tissue frequently present before the onset of exophthalmic goiter. In the Mississippi Valley where the incidence of endemic goiter is high, about 30 per cent of cases of exophthalmic goiter are superimposed on adenomatous goiter."

The subsequent development of this new type of tissue in adenomatous goiter is described by Plummer as indefinite. "Little is known regarding the duration of the normal life of the vesicles and the systematic development of new vesicles to replace those exhausted. The interest of the clinician and the pathologist centers largely in the development of groups of new acini that cannot be considered normal. Woefler contributed much to the subject of adenomas of the thyroid and made the observation that they develop from fetal rests. That anyone has actually traced the development of new acini from embryonal tissue is open to question. The groups of new vesicles may be very circumscribed and few in number, or distributed widely throughout the gland. The tissue may be encapsulated (true adenoma) or nonencapsulated (adenomatosis). In many cases a sharp distinction between encapsulated and nonencapsulated tissue cannot be made. That there is some difference in the factors entering into the histogenesis of nonencapsulated adenomatous tissue, widely distributed throughout the thyroid, and circumscribed encapsulated adenoma cannot be questioned. Under the terms 'adenomatous tissue' or 'adenomatous goiter' both types are included. In some adenomatous tissue, vesicles in all stages of development may be observed. The lumina of the so-called fetal acini contain no colloid and the cells present the general appearance of not having functioned. The fully developed new vesicles show the same histologic evidence of function as the normal vesicles and hence cannot be distinguished individually from the vesicles of the surrounding normal gland tissue. Depending on the relative number of adult vesicles, adenomas are classified as fetal or adult. In many adenomas

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high percentage of all the vesicles contain colloid and the new tissue is termed colloid adenoma. An isolated section of such tissue may not be distinguishable from the surrounding normal or colloid-distended thyroid. . . ."

"Two theories prevail regarding hyperfunctioning adenomatous thyroid: first, that the adenomatous tissue elaborates and delivers an excess of thyroxin; and second, that it in some way stimulates the surrounding thyroid tissue to hyperfunction. Although the questions must still be considered open, the evidence accords best with the theory that the adenomatous tissue hyperfunctions. To avoid this question in goiter classification, I have used the term hyperfunctioning adenomatous goiter which, so far as this point is concerned, is noncommittal. Irrespective of the question of which type of tissue furnishes an excess of thyroxin, there is no doubt that the adenomatous tissue actually elaborates thyroxin and stores colloid and iodin. In the following discussion of adenomatous goiter, the facts may be coördinated with either theory; however, I have assumed that the adenomatous tissue hyperfunctions.

"In most cases adenomatous goiter has its inception in colloid goiter. The embryonal cells seem to be stimulated through the same mechanism that forces the gland to maintain a normal level of thyroxin in the tissues. Possibly we should look on adenomatous tissue somewhat as a compensatory attempt. Such a theory does not eliminate the possibility that the formation of the new tissues may in some or all instances be determined by local irritants. Early in its life history adenomatous tissue cannot function. A number of observations suggest that it can elaborate and store colloid long before it can elaborate and store thyroxin. Only rarely are the factors such that the adenomatous tissue will function, at least to the point of causing hyperthyroidism, before the latter half of the third decade of life, although as a rule, it is palpable in the second decade. Only 5 per cent of the hyperfunctioning adenomatous thyroids coming under observation at the Mayo Clinic are in patients under thirty years of age. These constitute about 5 per cent of all adenomatous thyroids resected in patients under the thirtieth year. Sixty per cent of all adenomatous thyroids, resected in patients after the sixtieth year of life, are hyperfunctioning. The average interval between the time the goiter is first noticed and the onset of hyperthyroidism, including only those that hyperfunction before coming under observation, is seventeen and six-tenths years. Although the normal stimulating mechanism seems to be a factor in the inception of adenomatous goiter, once this tissue has started to function it does so erratically without relation to the demands of the organism. This observation is borne out by the fact that the basal metabolism drops to normal, but not below, within eighteen days after resection of the adenomatous tissue and there is no tendency to recurrence of the hyperthyroidism.

"It may readily be conceived that in this postnatally developed tissue the mechanism of coördinating its functional activity with the demands of the body is not fully developed. There is no apparent reason for the onset of hyperthyroidism in the majority of cases. It may be inferred that the adenomatous tissue has an inherent tendency to hyperfunction which is favored by various factors. The increased rate of exhaustion of thyroxin and the resulting elevation in the intensity of stimulation of the thyroid, which we have reason to assume exist in conditions such as essential hypertension, pregnancy and pituitary disease, probably favor the development of adenoma and not infrequently excite adenomatous thyroids to hyperfunction. In these cases the tendency to store colloid is, in general, inverse to the tendency to hyperfunction."

There has been no final acceptance of the duality of these conditions, however. Grouped on either side are equally well known authori-

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ties. Some consider toxic adenoma a distinct entity, others regard it simply as a phase of true exophthalmic goiter. Ginsburg's (*loc. cit.*) conception fairly represents the latter view.

"In recognizing toxic adenoma as a clinical-pathologic concept, I wish to stress strongly that neither clinically nor pathologically do I perceive any fundamental distinction between toxic adenoma and exophthalmic goiter except as the variation of a single disease. Nevertheless, for practical diagnostic and therapeutic reasons, the recognition of this variation is important, for in toxic adenoma the ocular signs are rarely present, the adenoma or adenomas may be small and readily disregarded if stress on this variation in thyrotoxicosis is omitted from the medical literature.

(*Continued on page 36*)

A Contribution to Kottmann's Reaction

(Translated from the article by Dr. Emil Walder, *Mitt. Grenzgeb. Med. u. Chir.*, 1926, 39 : 626, No. 4/5.)

By special permission of Dr. Emil Walder and of the publishers of "Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie". It forms a part of the collection edited by Prof. F. de Quervain. — Editor.

(Continued from Vol. XIII, No. 6)

In this tenfold stronger concentration of the reagent probably the albuminous substances of the serum, in their function of dispersing agent, result in the ensuing colloidal silver iodide, and the silver is so strong in the background that quite possibly one sees a reaction totally differing from the Kottmann reaction. In so strong a concentration it is possible that most of the silver iodide formed does not remain as a colloidal solution, but instead precipitates out directly.

In addition to the already mentioned difficulties and sources of error of the Kottmann reaction we were led to another point, namely, to the study of the internal mechanism of the reaction by the circumstance mentioned at the beginning that the result of the reaction is in high degree dependent on the succession of addition of the reagents. In this way we hoped to obtain at the same time a clearer insight into the nature of the reaction. In regard to it this also happened to give an experimental proof for the interpretation which Kottmann gives the reaction, by another route. In this respect a colloid chemical work of Lottermoser came to our assistance which states the following:

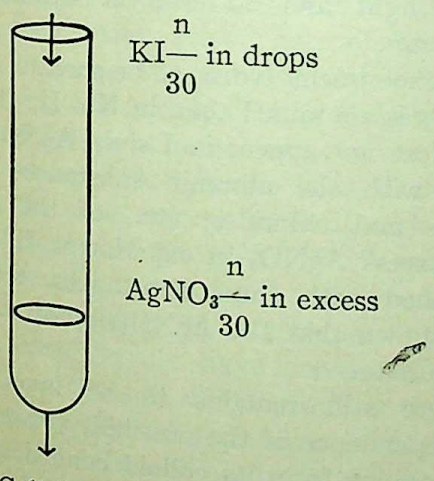
If we add potassium iodide in drops to silver nitrate with shaking, dissolved colloidal silver iodide is formed in which the silver ions present in excess are adsorbed. There accordingly arises a positive charged colloid to which we can give the following formula: $\boxed{AgI.}\ Ag.+$. The dissolved colloid state of this combination is related to a positive superfluity of Arg. nitr.; as soon as we have added the equimolecular amount of potassium iodide, everything is precipitated out as silver iodide. If we do the reverse, we add silver nitrate in drops to a solution of potassium iodide with shaking, then dissolved colloidal AgI likewise arises, but this time with adsorbed iodin ions, hence a negative charged colloid which may be represented schematically thus: $\boxed{AgI.}$

We utilized these facts in the Kottmann reaction. In the first case there accordingly arises the positive charged AgI with adsorbed silver ions. If we add hydrochloric to this, the Ag ion loosely adsorbed in the

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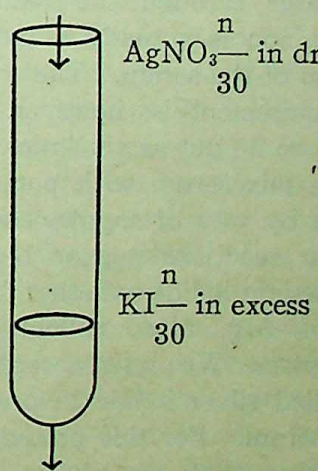
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is immediately extracted, that is, reduced to metallic silver, which may be recognized by the blackening immediately appearing. The negative charged colloid in which the silver is disguised, that is, is found in chemical combination with the iodin, is only very slowly reduced by hydrochinon. We can, therefore, enlarge our conception somewhat if we consider that during the addition of potassium iodide to silver nitrate there is a point where the colloidal iodide of silver has adsorbed a maximum of silver ions, where accordingly, in other words, there is a maximum of ion colloid in solution as disperse phase. If we add more potassium iodide, then the precipitation of undissolved silver iodide begins, since the iodin ions of the newly added potassium iodide unite with the adsorbed silver ions and the electrical charge which the colloid held in solution accordingly vanishes. The adsorption combination is broken up and the silver iodide is precipitated. These colloid salt solutions are very unstable since it is a question of pure colloid solutions without protective colloid, and it is probable that only the positive or negative charge which these colloids receive through the adsorbed Ag or iodin ions maintains them in colloid state. It seems to us very possible that impure works (sweat colloid, alkalin splitting up of glass) can favor the precipitation of these very unstable formations. Provisionally we believe that we have purely empirically come closest to the optimal point where most Ag ions are adsorbed in the colloid AgI (perhaps this point may be determined mathematically on the basis of Freundlich's absorption law) in such a manner that we add 3 c. c. of a 30 normal potassium iodide solution in drops with shaking to 5 c. c. of a 30 normal Arg. nitr. solution. These amounts correspond approximately to those given by Kottmann. In most cases we have then none at all, in other cases a beginning microscopically visible precipitation in flakes of an "undissolved" silver iodide. From this mixture we very rapidly pipetted off 0.5 c. c. and added this by mixing to 1 c. c. serum, light with 400 candles for 20 minutes and later add 0.5 of a freshly prepared 0.25 per cent hydrochinon solution, again mix and then read every five minutes for a half hour. We can summarize both mechanisms into one outline:



Colloidal [AgI.] Ag+
Addition of Hydrochinon

Immediate Reduction
(Immediate Blackening)



Colloidal [AgI.] I—
Addition of Hydrochinon

Very Slow Reduction
(No Blackening, Only Blue-Gray Coloration)

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In this way we hoped to obtain, therefore, a similar reagent for all sera, if not ideal, at least as constant as possible; we were, however, very conscious that these ionic colloids represent very sensitive, exceedingly unstable formations.

Our procedure is to be differentiated from that of Kottmann in that we add the finished AgI. Ag^+ to the serum, whereas according to Kottmann potassium iodide is first added to the serum, wherein Kottmann to be sure does not make any statement whether the potassium iodide should be mixed with the serum and then first the $AgNO_3$ should be added or whether it should be mixed first after the addition of the Arg. nitr. These things are of very great importance from the colloid chemical viewpoint and in our opinion can be decisive for the result of the reaction; the sequence of the addition of the reagents, of the time in which they are mixed, even the intensity of the mixture, play a great role in such reactions. It would, of course, be ideal to let the AgI. Ag^+ arise directly in the serum adsorbed in the serum colloid, since one would then have a better guarantee for the fact that the dispersion of the colloid silver arising later through the reduction through hydrochinon is actually a measure for the dispersion of the serum. The realization of this requirement is, however, very important since we do not as yet know what occurs when we mix serum with potassium iodide and then by way of supplement add Arg. nitr., what reactions appear between serum and potassium iodide, whether following addition of Arg. nitr., colloid silver iodide actually arises. We prefer, accordingly, to mix the colloid silver iodide in prepared form with the serum. For this procedure it was determinative that we obtain (after thorough experimental testing of each conceivable sequence of the combination of serum and reagent in the above mentioned type) the most constant results in harmony with the clinical history of the cases, in which in the above mentioned way certain colloid silver iodide was added to the serum. S another factor strengthens us in our p cedure: We thought of the possibility t relations might exist between the gold co and the Kottmann method (protective tion) and in the gold count method the col is also mixed with the serum in prepa form (colloid gold). In order that, acco ingly, a reduction in sufficiently mark measure and in conceivable time appea we must allow the above mentioned A Ag^+ to arise; potassium iodide must, the fore, be added in drops to the silver nitra and the latter must be present in exce Now the following objection could be ma since hydrochinon also immediately redu silver nitrate, then in the Kottmann re tion not the AgI. Ag^+ is reduced but the cess $AgNO_3$. We also took this objecti into account and performed extensive e periments of which we mention only t following here:

I. Serum 1 c. c. plus $AgNO_3$ (0.5 p cent) 0.3 c. c., light and addition of hydr chinon: no reduction.

II. Serum 1 c. c. plus $AgNO_3$ (0.5 p cent) 0.3 c. c. plus KI (0.5 per cent) 0. c. c., light and addition of hydrochino reduction.

In experiment No. I, to be sure, more fr $AgNO_3$ is contained than in No. II. Reduc tion does not appear in I since $AgNO_3$ com bines with the albumin substances, ph phates and chlorides, etc., of the seru The excess $AgNO_3$ in experiment II is al combined with these substances, therefo it is shown that the $AgNO_3$ is not the su stance reduced.

There still remains to be investiga the dependence of the possibility of reduci hydrochinon from its colloid condition, fr the alkalinity of the medium or of the and OH^- ionic concentration and the in fluence of the percentage albumin conte of the sera. The latter could be estimate rapidly by the refractometer. Moreov the gold count of the sera must be determin

parall we ha see w both the ar used i We the re whethe exopht for cre reactio the ma cally, a tion. If t cording it wou course to set specific conditi In th followi The mann in the conditi wrappe glass; was clo kept in goiter exactly before always took pla that it fluence expressi culation agulate centrifug tion of thalmic all sera sera we

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parallel with the Kottmann reaction — we have already referred to this point — to see whether relations do not exist between both methods (protective action). Finally, the amount and concentration of reagents used in the reaction appear to be too large.

We now tried to represent the course of the reaction graphically and wished to see whether we could obtain definite curves for exophthalmic goiter on the one hand and for cretins on the other; the course of the reaction is nevertheless too inconstant in the majority of cases; to represent it graphically, accordingly, has above all no signification.

If the reaction were once improved according to the hitherto mentioned viewpoints, it would perhaps be possible to record the course of this graphically and for example to set up definite types of curves, as it were specific curves, for different pathological conditions.

In the investigation we proceeded in the following way:

The blood was drawn by means of a Wassermann needle from the obstructed arm vein in the morning with the patient in fasting condition, and collected in a sterile test tube wrapped in black paper and of ordinary glass; following the removal the test tube was closed with sterile cotton wadding and kept in the dark at room temperature. The goiter venous blood serum was drawn in exactly the same manner when it took place before luxation of the goiter, which was not always possible, to be sure; the luxation took place, however, in so sparing a manner that it could hardly have an essential influence on the result of the reaction through expression of thyroid substances into the circulation. We then allowed the blood to coagulate and in very many cases we had to centrifuge it owing to the insufficient separation of serum there and coagulum (exophthalmic goiter); we centrifuged systematically all sera following coagulation. Hemolytic sera were not used. By means of glass pipettes 1 c. c. was pipetted in diffuse daylight into small test tubes of ordinary glass and identical color, identical lumen and identical thickness of wall as the test tube of the standard; for each new serum another freshly cleaned pipette was used. Test tube and pipettes were rinsed with water following usage, mechanically cleaned, laid in dilute hydrochloric acid solution for a time, washed with distilled water and alcohol, then dried with ether and warm air and kept closed with a clean cork stopper.

In an ordinary test tube previously treated in the same manner, we prepared the reagent in which we allowed 3 c. c. of a 30 normal potassium iodide solution (chemically pure) to drip in drops with shaking into 5 c. c. of a 30 normal silver nitrate solution (chemically pure), immediately before any precipitation was formed, we pipetted off several c. c. of this mixture and then allowed 0.5 c. c. reagent to be added in drops to 1 c. c. of serum with careful mixing. The test tube was then closed with a clean cork. We now lighted with 400 candles at a distance of 25 cm. for exactly 20 minutes and then added 0.5 c. c. of a freshly prepared 25 per cent hydrochinon solution (dissolving of 0.25 gm. crystallized hydrochinon in 1.00 Aq. dest.), mixed again and then took readings every 5 minutes for a half hour. At the beginning we made a reading after ¾, 1, 2 and 3 hours, but for the most part the reaction was at an end after one-half hour. The mixing always took place with test tube closed with cork, never with finger pad closing, owing to the possibility of the disturbing influence of sweat colloid. All reagents, silver nitrate, potassium iodide, hydrochinon, were kept in dark brown bottles to protect them from decomposition with light. The pipetting off was always performed with diffuse day light; in the mid periods (following the pipetting off, between the readings during the reaction in progress) the sera was placed in a dark case. At the beginning we tried to carry out everything in the dark

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room but this was not successful; the pipetting could not be performed exactly enough in the red light and above all reading, which we made with the aid of Sahli's hemometer (left Kollargol standard, right serum), was impossible with red light. We needed an extremely intense light with the markedly browning sera and so we used the 400 candle transformer as source of light for the reading. In this way the periods during which the sera were exposed to the day light or artificial source of light (reading) were exceedingly alike; during the intervals the sera remained in the dark.

Of each serum, according to the amount, 2 to 4 reactions taking a parallel course with one another, were undertaken and the arithmetical mean taken as result. If the individual tests were too markedly divergent, the experiment was suspended and new [illegible] prepared. All sera were always exam[illegible] on the same day for the most part betw[illegible] 4 and 7 o'clock in the evening; the ven[illegible] blood of the arm was in general removed [illegible] tween 8 and 10 o'clock and the goiter ven[illegible] blood between 9 and 12 o'clock, mornings.

The following accounts of results proc[illegible] from cases which were treated in the w[illegible] described above. In about half of the ca[illegible] only after the termination of the experim[illegible] did we know from whom the sera originat[illegible] in the other cases a knowledge of the case w[illegible] not to be avoided before commencing t[illegible] reaction; we made an effort, however, [illegible] remain objective as much as possible. La[illegible] the result of the rat and of the gas excha[illegible] experiment was always known to us at o[illegible]

(*To be continued*)

Practical Therapeutics

Mammary Extract in Menorrhagia

IT has been generally recognized that during the development of organotherapy some animal tissues have been used in which a definite endocrine function has not been established. The undoubted therapeutic effects have justified their use and it has been assumed that from such tissues there may be obtained active chemical compounds exerting a positive pharmacological effect, but playing no essential part in normal physiology. The very powerful substances derived from the post pituitary lobe, one a marked pressor and the other an oxytocic, are examples of this. The mammary gland is another, although yielding derivatives much less active pharmacologically.

Mammary substance has had a somewhat limited use in medicine; nevertheless it has persisted and its use has been repeatedly described in the journal literature and in some of the textbooks. The incentive to search for evidence of physiological function exerted by such substances, however, always remains, for it seems difficult to believe th[illegible] the organism elaborates chemical compou[illegible] capable of exerting powerful selective acti[illegible] on various physiological mechanisms, a[illegible] that these compounds play no part in gene[illegible] physiology.

The use of mammary extract in m[illegible] orrhagia has not been constantly successf[illegible] but there has been sufficient evidence to b[illegible] lieve that it has some therapeutic value [illegible] various states of uterine bleeding. H. Vig[illegible] (abstract below) has suggested most of t[illegible] several theories used to explain the action [illegible] mammary substance. All of the mechanis[illegible] considered by Vignes appear to be insuffici[illegible] to explain the action of mammary substan[illegible]

This action of mammary suggests a p[illegible] sible relation of mammary to corpus lute[illegible] Such a relationship has been suggested a[illegible] the changes in the mammae at the menstr[illegible] periods and during pregnancy have been [illegible] lated to the corpus luteum.

The corpus luteum initiates remarkab[illegible] changes in the growth of endometrium bef[illegible]

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menstruation and is apparently necessary for the building up and organization of the uterine mucosa before a menstrual period. The influence of the corpus luteum increases from the period of ovulation (10th to 15th day) up to a few days before menstruation. It then rapidly degenerates and the follicular hormone (Allen-Doisy hormone) dominates up to the period of ovulation of the next cycle when the new corpus luteum begins its period of influence on the new cycle as above. If (as in pregnancy) a corpus luteum persists and continues its development menstruation and ovulation are inhibited. Leo Loeb has shown these effects experimentally — the corpus luteum inhibits ovulation and proliferation of the vaginal epithelium. Others (Corner and Allen) attribute to the corpus luteum a hormone which induces progestational proliferation of the endometrium and Parkes shows experimentally (mice) that corpus luteum is necessary for the whole gestational process (up to the time of normal degeneration of corpus luteum of pregnancy).

Papanicolau, Pearl and Surface, Payne, Van Peenan and Cartland have shown the presence in the corpus luteum of a hormone which exerts an inhibiting influence on estrus and menstruation, and Parkes and Bellerby and others have assumed that in pregnancy the corpus luteum gives rise to an estrous inhibitor action.

Now if we accept as true the effect of the corpus luteum on the whole process of gestation, proliferation of the uterine mucosa and the process of estrus (and this seems undoubted even if our knowledge is not complete) we can conceive of a mechanism through which mammary extract may act in controlling uterine bleeding for the relationship of the corpus luteum to the mammae has been described by numerous authors (Leo Loeb *et al.*) and it is possible that there may be a reaction of corpus luteum to these extracts. In any event the subject of mammary opotherapy is a suitable field for further investigation.

Mammary Organotherapy. — H. Vignes. (*Bull. gén. thérap.*, 178 : 439, Dec., 1927.)

The function of the ovary determines modifications in the mammary glands each month, which increase in case of pregnancy; these changes are therefore a part of the preparation for pregnancy; they consist in more or less intense congestion and more or less active division of the cellular elements. The phenomena observed are, of course, of ovarian origin. That this is so has been demonstrated by the possibility of reproducing the congestion and cellular multiplication by injections of folliculin, by the determination of analogous changes in the castrated male guinea-pig following ovarian grafts, finally by the association of castration with an atrophy of the mammary gland.

Amenorrhea is sometimes associated with secretion of milk. In certain cases of false pregnancies with amenorrhea and abdominal obesity, an abundant secretion of milk has been observed. Certain amenorrheic young girls, apparently normal otherwise, lose an abundant quantity of milk each month for several days. Secretory outbursts have occasionally been observed at the menopause.

Painful mammary hypertrophy is often caused by ovarian disease without amenorrhea. Leriche published the case of a woman of 37 years with very painful hypertrophy of the breasts since puberty and menorrhagia at the same time. A laparotomy was performed and two large tubo-ovarian cysts were extirpated. Following the operation the breasts decreased in size and pain disappeared.

Dysmenorrhea often has an effect on the mammary gland and Dalché even notes a comparative frequency of mastitis and adenomas in such cases.

Certain authors have suggested the existence of a mammary internal secretion: the results of mammary organotherapy have especially served as basis for this hypothesis. Certain facts may be interpreted as being the consequence of an action exerted by mammary function on the ovary: (1) Many women do not menstruate during the months of lactation and it is among these that the majority of good nurses are found. (2) The suppression of lactation speedily brings on menstruation. (3) The fertility of nurses is lessened during the whole period of lactation.

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The Doctor's Page



JEAN-HENRI DUNANT
(1828-1910)

The Red Cross Society has attained such renown and its services have been so universally accepted, that the stormy background of its origin and the tedious process of organization are almost lost to us. The founder the Red Cross Society, Jean-Henri Dunan spoke significantly when, after the work the society was well started, he said, "Ish

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retire into the background; the work is well under way; I am but a tool in the hand of God." Dunant desired always to be an unidentified volunteer worker unless the cause he essayed required that he associate himself with the illustrious family or the social rank to which he belonged.

Dunant was born in Geneva, May 8, 1828, in a noteworthy family consisting of five children, of whom the youngest, Pierre Louis, was to become a well-known instructor of Hygiene at Geneva; a father, Jean-Jacques Dunant, who held several important posts in the city and was active in public welfare work, and a mother, Anne-Antoinette Colladon, also of a distinguished lineage. One relative, Daniel Colladon, was the physicist known for his investigations on the transmission of sound under water and more especially for the invention of compressed air drills which made possible the opening of the Alps to the railroad.

With these inspirations before him, it is scarcely to be wondered that Jean-Henri contributed also to the already resplendent family name. As a child he was extremely solicitous of the welfare of others, and thoughtful of all those about him. He was always helping the less fortunate people in life, and gave much of his time to educating and teaching the inmates of the prison on Sundays. The slavery question, especially in the phases presented by Harriet Beecher Stowe so attracted his attention that he wrote an essay "L'esclavage chez les Musulmans et aux Etats-Unis" (1863, Geneva).

For a livelihood Dunant chose commercial occupation, but for a hobby he pursued studies in archeology, ethnography and history. While engaged in business in Algiers and Tunis he wrote a treatise "La régence de Tunis," a scholarly study of the history, government, finances, judicial system, naval affairs, climate, and people of Tunis, well supported with authoritative references. This work obtained for the author recognition in several learned societies and especially a membership in the "Société d'ethnographie" in Paris.

During the struggle of 1858-59, for the unity of Italy, in which France, Austria and Italy were intensely involved, Dunant chanced to be traveling in Southern Europe. Just after the battle of Solferino, June 24, 1859, he was at Castiglione, where the charitable inhabitants were helping to clear away the remains of the several armies, both wounded and dead. The awful gruesomeness of the battlefield, the inadequacy of the military medical service and the agonies of the wounded struck him so forcibly that he at once set himself to guide the group of voluntary workers to render first aid. It was not long before the cognomen of "Monsieur Blanc," by which name Dunant was called because of the white uniform he wore, spread far and wide. It is particularly significant that he made no distinction in the treatment of the wounded, whether Italian, French or Austrian — they were "all brothers." As a result of these experiences Dunant wrote "Un souvenir de Solferino" which achieved world fame and in which may be found the seeds of the idea of the Red Cross Society.

Herein Dunant depicts in great detail the clash of "two belligerent armies" and the disaster they leave behind them. He questions "Would it be possible to establish in every country of Europe aid societies whose aim would be to provide, during war, volunteer nurses for the wounded, without distinction of nationality"? Such a society would begin to function as soon as war was declared. "Societies of this kind . . . should obtain the favor of the authorities of the countries where they are created, and beg in case of war, from the sovereigns of the belligerent powers the permission and facilities necessary to carry out their purpose. . . . The moment of commencement of war the committee would call on those persons who desire to dedicate themselves, for the time being, to this work, which will consist in helping and nursing, under the guidance of experienced physicians . . ." ("Un souvenir de Solferino" translated by Mrs. D. H. Wright, 1911, Philadelphia). Later a clause was inserted into these principles which stated that the society "could be of great help in epidemics or great disasters such as conflagrations and floods."

On February 9, 1863, the "Société genevoise d'utilité publique" appointed a committee to prepare the way for such a society, and made Dunant its Secretary, in which capacity he rendered not only official but also personal services in the cause he had inaugurated. He was favorably received by Napoleon III, Crown Prince Frederick and Queen Augusta as well as by other famous personages. The work of this committee

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Medical Subjects by Famous Masters



"THE ALCHEMIST'S LABORATORY," by Thomas Wijck (1616-1677)

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Editorial Comment

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Hyperinsulinism

THE term hyperinsulinism is occasionally encountered in the literature. Usually it is applied to those conditions of hypoglycemia in which a blood sugar considerably below normal is not attended with the usual symptoms of such a condition. The number of cases which display this phenomenon is rather large and a satisfactory explanation has not yet appeared. The theory of excessive insulin production is purely conjectural, with almost no experimental work to support it. Most of the untoward symptoms of excessive insulin dosage have been attributed to the resulting hypoglycemia. Yet, a sufficiently large number of cases has been reported in which the symptoms were not at all, or only slowly relieved by administration of sugar and it seems clear that the degree of hypoglycemia frequently does not parallel the symptoms. Excessive insulin dosage produces not only marked lowering of blood sugar but may also apparently induce some toxic symptoms not necessarily dependent upon the hypoglycemia.

The relation of lowered blood sugar unassociated with symptoms can not at the present time be ascribed to excessive insulin production.

The use of the term hyperinsulinism by John (abstract below) is limited to the effects of insulin overdosage. While it is not established that insulin treatment tends to restore the function of the pancreas to elaborate insulin, the fact is well known that insulin dosage may be frequently reduced. It is possible that the substitution effect of administered insulin gives a rest period to the defective pancreas and spontaneous regeneration may occur. Hyperinsulinism (apart from administered insulin) as a clinical entity has not been proved.

Hyperinsulinism. — H. J. John. (*Surg., Gynec. and Obstet.*, 44 : 190, Feb., 1927.)

The term hyperinsulinism is employed to indicate a group of symptoms which are caused by a prolonged overdosage with insulin.

When a diabetic patient is placed on a certain insulin dosage, the amount being just sufficient to control his hyperglycemia and glycosuria, it does not follow that this dosage should be maintained during the whole course of treatment. The amount of insulin may have to be increased as time passes, or it may have to be decreased. If the endogenous insulogenic function of the patient improves and more endogenous insulin is provided, then less exogenous insulin is needed. In such a case the daily dosage of insulin which was prescribed at first becomes an overdose, and, if it is continued, symptoms of either mild or severe hyperinsulinism may appear. Because of the striking similarity of these symptoms to those of hyperthyroidism, a wrong diagnosis may easily be made and the patient subjected to a thyroidectomy without securing any relief from his symptoms. Therefore, hyperinsulinism should always be ruled out by a blood sugar examination, if hyperthyroidism is suspected in a patient who is being treated with insulin.

The treatment of hyperinsulinism is simple — merely the discontinuance of insulin. If

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this be insufficient the administration of some food between meals will be effective. Voracious hunger a few hours after the administration of insulin usually indicates hypoglycemia.

Urinary examination alone is not a sufficient basis for judgment in a case of diabetes in which insulin treatment is employed. In such a case if the patient happens to have a low renal threshold he may continue to eliminate sugar even in the presence of hypoglycemia. Without a glucose tolerance test such a condition might be interpreted as due to insufficient insulin dosage, and the insulin treatment would be continued and the dosage might even be increased, a course which would inevitably lead to hyperinsulinism.

Insulin and Hypoglycemia. — Editorial. (*J. Am. Med. Assn.*, 89 : 971, Sept. 17, 1927.)

The most noticeable feature of overdosage with insulin is the resulting hypoglycemia. The widespread custom of making estimations of blood sugar for diagnostic purposes has brought to light the fact that hypoglycemia is by no means as uncommon as has been assumed. Some observers have been inclined to attribute many of the instances of hypoglycemia to what they designate as hyperinsulinism. However, it is questionable whether hypoglycemia and hyperinsulinism are invariably closely interrelated. Harrop has demonstrated that the administration of carbohydrate to unconscious persons in insulin reactions does not always have the immediate prompt effect that has been anticipated. The degree of hypoglycemia apparently does not accurately determine the severity of the reaction, nor does the administration of sugar always relieve it. Recovery of consciousness may occur spontaneously even when the blood sugar is at a low level of concentration. Harrop regards it as probable that the toxic effects noted, especially the marked mental disturbances, may be due partly, or in some cases entirely, to some other action of insulin. These are possibilities that need to be recognized.

Thyroid and Growth

FREDERICK HAMMETT has made a number of substantial contributions to our knowledge of growth and the thyroid gland. In the article abstracted below he discusses the differential development of organs following thyroid and parathyroid removal. In this study he has compared the development of organs (the weight is taken as the measure) with body weight in animals in which both the thyroids and the parathyroids have been removed. These values have been plotted graphically. If the curve for any particular organ coincides with the curve of the body weight at any given point, there is no distortion of development. If it deviates there has been a differential value in development. Hammett has found that the lack of growth following thyroid and parathyroid removal is the result of essential under-nutrition and not of any specific glandular effect on growth.

"Hence the conclusion is justified that the difference in degree of growth response of the several organs in conditions of thyroid and parathyroid deficiency is, in general, due to specific organ constitution and the relation of this to the metabolic or nutritional level and not to any specific influence of glandular activity as such in the growth of the individual structure. Such is the essential basis of the distortion of differential development."

These conclusions are essentially in accord with those of Child in his theory of "axial gradients." Child conceives that at various points along the long axis of the body there is a series of differing metabolic rates. These points of mere qualitatively increased metabolism give rise to differences of development with a result which is qualitatively organs are formed by reason of the increased cell division and development contingent upon the differences of metabolic rate.

Child's experiments, however, were made on animals rather low in the animal scale (planaria) and it seems that in higher forms there is finally a stage of embryonic development in which the potential organs are inherent in certain cells or groups of cells. (Lo has shown that the germinal area of a left le may be transplanted to the right side be still develop as a left leg.) It is these primitive areas and embryonic organs that exhibit

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the individual differences of reaction to the general metabolic stimulant — thyroid secretion. These differences are well described and charted in the article by Hammett.

Generalizations from the Differential Development Observed in Conditions of Thyroid and Parathyroid Deficiency. — Frederick Hammett. (*Am. J. Physiol.*, 82 : 250, Oct., 1927.)

Distortion of differential development follows both thyroid and parathyroid removal. With the exception of the hypophysis, the submaxillaries, and possibly the spleen, this is not due to any specific relation of glandular functions to organ growth, but to the general metabolic disturbance induced by the deficiencies.

The growth of some organs is more resistant and that of others is more sensitive than that of the body as a whole. The basis of this differential reaction lies in the relation of the metabolic processes of the organs in question to the bodily economy as a whole. The distortion is consistent in direction and produces a distinctly modified type of structural organization.

Since it can justly be assumed that endocrine activity in general is largely concerned with the regulation of metabolism, it is not improbable that the incretory organs have been and indeed still are endogenous participants in the determination of evolutionary change in the organisms in which they are present.

Abstracts

Surgical Treatment of Goiter. — G. E. Aróstegui. (*Revista Méd. Cubana*, 37 : 1082, Oct., 1926.)

Goiter in all forms is becoming more frequent in Cuba. Colloid goiter of adolescence or congestions of the thyroid require prolonged medical treatment. All the other forms of goiter are exclusively surgical and require the cooperation of the internist for a prolonged pre-operative and post-operative medical treatment. The assistance of the laboratory technician for pre-operative and histological examinations is also requisite, pre-operative examination being indispensable in the preparation of the patient and histological, in the following up of operative treatment (as in some of the author's cases) with deep radiotherapy.

Non-toxic goiters are exceedingly benign and very easy to extirpate. Toxic goiters require the attention of a genuine specialist and the whole cooperation of the hospital staff.

Lugol's solution is a two-edged sword and should be used only by a specialist. It has, to be sure, within a short time reduced the number of interventions in cases of hyperthyroidism. Hitherto, the interventions numbered three or four, whereas today only two interventions, and at times only one, are practiced.

Ten cases of goiter were subjected to operation by the author within the last three months.

Classification of Acromegaly in Two Clinical Forms: Simple and Complicated (with Optico-Diencephalic Symptoms). — C. P. Waldorp. (*Semana Méd.*, 33 : 765, No. 38, Sept. 23, 1926.)

Following a detailed description of the benign and malignant forms of acromegaly, as established by Prof. Oskar Hirsch of Vienna, the author relates his own experiences in seven cases of acromegaly, five of which were subjected to deep radiotherapy. He concludes that:

1. The clinical classification of acromegaly (disease caused by eosinophil adenoma of the anterior lobe of the pituitary) in the benign and malignant forms proposed by Prof. Hirsch of Vienna, is the equivalent of maintaining the existence of two distant entities in a single disease, with or without the participation of the optic routes. The malignant character would be given by the existence of symptoms of compression of the optic pathways and would be frequently accompanied by the symptoms proper to the syndrome of adiposogenital dystrophy. (Fröhlich-Babinski Type). In Hirsch's opinion, cases of malignant acromegaly should be operated upon early.

The author's classification of acromegaly is clinically broader and he divides his cases as follows:

(a). Acromegaly without optico-diencephalic symptoms (simple acromegaly).

(b). Acromegaly with optico-diencephalic

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symptoms (complicated acromegaly), cases in which there may be: exclusive or predominant symptoms of alterations of the optic pathways or of the diencephalic centers (adiposo-genital dystrophy, polyuria, glycosuria, disorders of sleep, etc.).

2. With the exception of special contra-indications, the treatment to be given is, in the author's opinion, the following:

(a). In simple acromegaly (without optico-diencephalic participation): irradiation of the pituitary tumor, with radiotherapy pursuant of the old technique of Béclère, and pluri-glandular organotherapy adapted to each case, and if indications of syphilis exist, corresponding combined treatment. If the course of the disease is not arrested thereby and if symptoms do not subside, deep radio-therapy.

(b). In acromegaly with optico-diencephalic symptoms, the conduct which the author follows is this: if the case is of recent origin, deep radiotherapy; if three months have transpired without improvement of the visual field or regression of the diencephalic symptoms, he advises hypophysectomy by endonasal route. If superaggregated symptoms of the disease persist or recur after the operation, the author believes deep radio-therapy an urgent necessity.

In those cases in which the destruction of the pituitary has reached a maximum, great vigilance of the endocrine-vegetative system is required, in order to prevent the so-called pituitary cachexia.

Gynecomastia in the Male and Its Relationship to the Whole Constitution. — F. Prange. (*Arch. f. Frauenkunde u. Eugenetik.*, **12**, Nos. 1 and 2, 1926.)

In seven cases of gynecomastia the great variation of the sexual types and the multiplicity of the constitutional relationship of this intersexual phenomenon were pointed out. Its etiology must be sought in part in a peculiar hormone effect, which however, must meet with a heightened developmental preparation of the rudimentary mammary gland hereditarily fixed in the germ plasm, when a gynecomastia is to result therefrom.

Adiposity and the Ovaries. — H. Wintz. (*Zentr. f. Gynäkol.*, **50** : 964, 1926.)

The author made an exhaustive study of the relationship between ovarian function and obesity. After the menopause, as well as following castration in younger women, there appeared in the majority of cases a lowering of the basal metabolism, which frequently was accompanied by the laying on of fat. Administration of organotherapeutic preparations led almost always to a rise in basal metabolic rate and corresponding loss of weight. Ovarian preparations were for the most part sufficient; in other cases a pluriglandular preparation (thyroid, ovary) had to be utilized.

Metabolism Regulation. III. Contribution to the Nervous and Endocrine Influence on the Transformation of Fat in the Liver. — E. Wertheimer. (*Pflüger's Arch. f. d. ges. Physiol.*, **213** : 287, 1926.)

In the investigation of the regulation of the transformation of fat in the liver, the following resulted with regard to the action of the endocrine glands.

Insulin accelerated the transformation of fat in the liver; at the same time an increase in glycogen content took place. Also following adrenalin administration a marked transformation of fat could be demonstrated in the liver, whereas simultaneously new carbohydrate was formed.

Hypoplasia of the Genital Glands and Insufficiency of the Thyroid. — Stangonelli. (*Riforma med.*, No. 2, 1926.)

The author directs attention to a disease picture which has received little consideration which makes its appearance at the age of puberty, is associated with ascites, but must not by any means be mistaken for a tuberculous peritonitis. Essentially it appears in infantile individuals with manifest hypoplasia of the genital organs and insufficiency of the thyroid, who present the characteristic symptoms of status thymico-lymphaticus and in whom the abundant lymph consequent to endocrine disturbances appears as serous effusion into the abdominal cavity. In such cases, therapy has to curb the activity of the thymus gland and of the lymph system and has to strengthen the thyro-genital system through the administration of gonad and thyroid extracts together with the other hormones.

Thyroid Therapy. — A. Oswald. (*Terapia contemporanea*, **1** : 507, 1926.)

A broad field opens today for thyroid therapy. It is indicated in the treatment of myxedema in all its forms, in endemic cre-

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ism, at least in the form of thyrohypoplastic cretinism, which one can very well call endemic myxedema, as well as in the treatment of myxedemoidia, i. e., the aborted form of myxedema. Hypothyroidism represents a significant quota for thyroid therapy, with thyrogenous constipation, adiposity, chronic metrorrhagia, pregnancy nephritis, tendency to edema in pregnancy, edema of the menopause, psychic disturbances in the puerperium and in the menopause, hypothyroid cardiopathy, ulcerous dermatitis, if the manifestations should make their appearance in acne, furunculosis, chronic eczema or trophic disorders of teeth, hair and nails.

In the cases enumerated thyroid therapy is not only a substitution therapy but also a stimulative therapy, in which often the favorable effect of the treatment outlasts the suspension of thyroid therapy.

A broader field of application for thyroid therapy is found in diseases which are based upon a disturbance of metabolism. To this belong conditions of asthenic anemia without nervous etiology, avitaminosis, chronic articular rheumatism, arthritis deformans, true anemias, in which iron and arsenic only with the help of thyroid therapy lead to recovery, and defective callus formation.

Finally, thyroid therapy accomplishes good results in general dystrophic infantilism, in senility and sometimes in ectopic testicles and cryptorchidism, in reducing cures, true nephroses and edema of extrarenal origin, and in goiter (diffuse, parenchymatous and colloid) without Basedowian symptoms.

Contraindications to thyroid therapy are Basedow's disease, hyperthyroidism of every form, marked lability of the vegetative nervous system, decompensated heart failure, tuberculosis, chronic nephritis and severe diabetes.

In myxedema, one can, comparatively speaking, administer large doses: 0.2-0.3 thyroid desiccated substance once daily. In mild cases of myxedema, half the above dose once daily is sufficient, or the same (larger) dose every two days. If the appearance of hyperthyroidism is to be feared, it is well to administer only half doses every two days.

This dosage is also satisfactory for the symptomatic application of this therapy. In no case should the above given limits of dosage be overstepped, unless in reducing cures, under the supposition that the heart is sound and the vegetative nervous system is not overtasked. Then, double or triple the previously mentioned dosage may be given (two to three times daily 0.2-0.3 thyroid desiccated substance). The author advises against higher doses.

During menstruation the treatment should be discontinued. If symptoms of hyperthyroidism appear in the course of a treatment, the cure must be suspended and should first be continued after complete disappearance of the hyperthyroid symptoms with smaller doses.

Thyroid therapy must be continued for a long time. As a rule one obtains better results with small, long continued doses than with large doses continued over a shorter period of time. In complete myxedema treatment must be continued throughout the patient's lifetime. In hypothyroidism, the disappearance of hypothyroid symptoms sets a limit; in the symptomatic cures, the appearance of the desired effect of thyroid therapy. In recurrence of the disorders the treatment is again to be taken up.

Clinical Observations and Metabolic Investigations following Treatment with the Water-Soluble Folliculin. — Joseph. (*Archiv f. Gynäkologie*, **132** : 192, 1927.)

The author reports his experiences with folliculin in 20 cases. Five of these patients were amenorrheic for years — 2 to 8 years — and had already been treated without success with many ovarian preparations. In two patients transplantation of one ovary had been undertaken but with negative result. Moreover, two youthful patients who had been subjected to extirpation of the adnexa with conservation of the uterus, were likewise treated with folliculin; 8 patients with dysmenorrheic complaints and six more young patients who had been subjected to total extirpation for carcinoma.

Of the five patients with amenorrhea for years, menstruation again made its appearance in four, after an average of six weeks. Folliculin was injected daily. In one patient the structure of the uterine mucosa could be followed closely. Three weeks following curettage, the mucosa exhibited no change. Four weeks following initiation of folliculin therapy a definite growth of the glands, here and there also glycogen deposit was also demonstrated; again, after 3 weeks, regular gland epithelium with abundant glycogen

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content was to be determined. The patient now had regular menses. In one patient folliculin was without effect. The patient in whom the adnexa had been removed, had very severe symptoms of ovarian hypofunction, with an eczema intertrigo which could not be influenced by any special treatment (x-rays). Following twenty injections of folliculin the eczema disappeared; following the 28th injection the patient had a menstrual period lasting 2 days. In all 20 patients, the calcium content, blood sugar, cholesterin content and basal metabolism were examined regularly, at first before treatment and later following every 10 injections. In 13 of the 20 patients definite rises in calcium content were to be observed; the lower the calcium content at the outset of treatment, the greater was the rise. The increase amounted on the average to 2 mgm. per cent. In patients without rise in calcium content the clinical manifestations also remained uninfluenced.

In 15 cases a distinct increase in blood sugar was to be observed, most markedly following intravenous injection of folliculin. With regard to the cholesterin content a uniform action is not demonstrable. The basal metabolism changes in a favorable sense. In eight patients with very low basal metabolism a rise up to 40% occurred. On the other hand, in 6 patients with high basal metabolism it fell to 35%.

The Intestinal pH in Experimental Rickets. — Bernard L. Oser. (*Journal of Biological Chemistry*, **80** : 487, Dec., 1928.)

Bernard undertook experiments in order to examine the feasibility of the fecal pH test as a measure of vitamin D potency. Also, to study the relation of the hydrogen ion changes to the etiology of rickets.

He concludes that aside from its lack of specificity, it would seem that the fecal pH test for vitamin D potency fails to approach a quantitative ideal for these reasons: There is not sufficient uniformity in the reaction of the feces to permit the establishment of a border zone to distinguish between normal and rachitic rats; there is considerable fluctuation from day to day among individual rats in the fecal pH value, even while the diet remains unchanged; the time response of different rats to the experimental diets is not sufficiently constant.

As a qualitative indication of the presence of vitamin D the test is satisfactory provided other factors which influence the reaction (such as Ca:P ratio, acid:base ratio, inanition, etc.) are controlled.

The addition of acidogenic or alkaligenic salts to the Steenbock and Black rickets-producing diet, in the amounts used by Zuckerkandl, Johnson and Barnett was without effect upon either the promotion or inhibition of rickets in these experiments. Although these salts diets appeared to possess no influence on the intestinal pH values not shown by the unmodified basal diet, a positive effect of greater proportions of the salts must not be excluded.

The decreased alkalinity of the colon contents of the normal rat is regarded as related to phosphorus reabsorption which normally occurs at that portion of the intestinal canal; whereas the sustained increase in alkalinity at this region in the rachitic rat appears to be associated with inadequate phosphorus reabsorption. Since even the rachitic rat has been shown to absorb and utilize calcium to a certain degree, it is probable that the primary etiological disturbance in rickets is the loss of phosphorus from the lower bowel, and the consequent decrease in the level of this element in the blood plasma.

Fasting, being accompanied by inadequate calcium intake, may affect recalcification because of the conservation or restoration of the inorganic phosphorus level in the bathing fluid of the bones.

Oser says in an addendum that following the preparation of the foregoing, a paper by Shohl and Bing appeared, in which similar conclusions are reached regarding the value of the fecal pH test in rickets. He adds that it is interesting to note their failure to reduce fecal pH by irradiation of a modified Steenbock diet.

Pancreatic Function. — Seizaburo Oda, Ehchi Sakurai, Tsunamoto Imazu and Kwanichi Kuramochi. (*Archives of Internal Medicine*, **42** : 270, Aug., 1928.)

The authors have devised a method making possible a reliable and accurate estimation of the pancreatic function. The patients used in the experiments were adults who had been under careful observation in the hospital. Most of them showed only mild clinical symptoms, such as constipation and neurasthenia, and were thought to be free from pancreatic involvement.

By this method the enzymatic efficiency for a fixed time is determined by multip

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ing the degree of enzymatic activity by the amount of duodenal return collected. The authors, after considering the difficulties and failures, chose a three hour method, which seems most reliable. The normal value thus obtained from a study of 50 patients is from 30 to 120 kilo-units for trypsin, and from 50 to 300 kilo-units for amylase and lipase. The average value of the normal results becomes 70 kilo-units for trypsin and 140 kilo-units for amylase and lipase. Alcohol, ether, water and hydrochloric acid are applied as stimulants. Alcohol and ether stimulate the outflow at the beginning, but do not have a marked influence on the whole enzymatic efficiency in a three hours' collection, while hydrochloric acid seems to increase the output slightly.

The degree of enzymatic activity of the duodenal return collected in a short period gives but little information concerning the pancreatic activity. However, if the estimation is carried out fractionally every half hour or every hour separately for 3 hours, and the highest value is found, the result is fairly consistent, being over 500 units for trypsin and over 600 units for amylase and lipase. Age seems to have some influence on the enzymatic efficiency; it is highest between the ages of 20 and 40, and is somewhat less before and after those ages. The influence of sex is more obvious, the enzymatic efficiency being much less in the female sex. The amount of the duodenal return does not seem to be influenced much by age in patients from 16 to 62 years old. The influence of sex is apparent, the amount being much less in females. The amount of pigment ranges widely. It is judged that the amount of the bile pigment increases with age and shows higher values in the male sex.

Rôle of the Thyroid and Parathyroid Glands in Vaso-Motor Reflexes. — Swale Vincent and J. H. Thompson. (*Journal of Physiology* (London). **66**: 449, Dec. 20, 1928.)

These authors have endeavored to investigate the parts played, if any, by the various endocrine glands in the body in relation to vaso-motor reflexes and associated phenomena. This paper deals with their experiments relating to the thyroid and parathyroid glands in particular.

Decerebrate cats in which the thyroid and parathyroid glands are removed show after a certain lapse of time an abnormally large pressor response upon stimulation of skin, muscle or intestine. The authors describe two crises which may occur. Under certain conditions this abnormality can be combated successfully by the injection of parathyroid extract (Collip), and also by double adrenalectomy.

Reasons are advanced to show that the increased pressor response is due to liberation of large quantities of autacoid substance and is not owing to any depression of the vaso-motor reflex. The authors consider the secretion of this autacoid substance to be stimulated by some substance liberated by the adrenal glands, and that one of the functions of the parathyroid glands (and possibly the thyroid also) is to limit the secretion of autacoid pressor substance by control of the aforesaid stimulating agent.

A Non-Specific Pressor Principle Derived from a Variety of Tissues. — J. B. Collip. (*Journal of Physiology* (London), **66**: 416, Dec. 20, 1928.)

Collip describes a method for the production of extracts containing a powerful pressor component, a wide variety of tissues being used as a source.

The pressor extract derived from the prostate gland has been found to be essentially different in character from pressor extracts obtained from other tissues studied.

The non-specific pressor substance has an interesting pharmacology.

(a) It does not affect blood sugar.

(b) The pressor response is enhanced by small doses of ergotamine. A large dose may cause reversal of the pressor action.

(c) The pressor effect is antagonized by the intravenous injection of small amounts of cocaine hydrochloride.

(d) Atropine does not affect its action.

(e) Nicotine does not diminish the pressor effect but may cause enhancement.

(f) Small amounts have little or no effect upon isolated intestine, uterus or heart. Large doses are depressant.

(g) The pressor response (both height and duration) is directly related to the size of dose within certain limits.

(h) Repeated injections at short intervals do not alter the character of the pressor response.

Whether the active principle exists as such in the tissue, or is produced during the process of making the extracts, is not established.

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Relation of the Endocrine and Vegetative Nervous System to the Production of Disease in the Skin. — Harvey P. Towle and J. L. Grund. (*New England Journal of Medicine*, **199** : 1267, Dec. 20, 1928.)

Dermatologists are becoming slowly convinced that in disturbances of the endocrine system or in disturbances of the vegetative nervous system may often be discovered the foundations on which subsequent disease has developed.

John, who has studied the carbohydrate metabolism in hyperthyroidism, states that there is no specific dextrose tolerance curve for hyperthyroidism but thyroidectomy lowers the total metabolism and in consequence improves the carbohydrate tolerance. He, moreover, believes that hyperthyroidism plays a fundamental etiologic role in the disturbance of the endocrine equilibrium which constitutes the diabetic syndrome. Patients with hyperthyroidism, in whom a frank diabetic condition of severe type is not present, but merely a mild degree of disturbance of the carbohydrate metabolism, John considers to be functional diabetics. To these patients the administration of thyroid is not without danger.

Usher examined 106 cases of eczema of which he found that 54.7% had some degree of disturbance of the carbohydrate metabolism. Rabinowitch obtained about the same figures in a study of 713 non-diabetics. Usher found 40.5% of his eczematous patients had a delayed assimilation with or without a diminished carbohydrate tolerance as compared with 20% in a non-eczematous group. When considered in conjunction with John's studies, Usher's acquire added significance.

From the work of these two men it is seen that hyperthy oidism favors carbohydrate intolerance (John); that carbohydrate disturbance favors eczema (Usher); that in the presence of such disturbance, the skin reactivity is often increased; and that bacterial activity on the skin is favored in direct proportion to the amount of sugar in the sweat.

In view of the frequent administration of ovarian extracts it is interesting to know that in a study of 150 cases of various functional disturbances of the ovary Hornung found that the ovary did not regularly exercise any direct influence either on the basal metabolism or on the specific dynamic action of food stuffs.

Effect of Insulin on the Distributio of Non-Protein Nitrogen in the Blood. Stanley E. Kerr and Vartan H. Krikori (*Journal of Biological Chemistry*, 81 : 4 Feb., 1929.)

The authors, in view of Sokhey and Alla report that insulin causes an increased exc tion of nitrogen in the urine, deemed it wo while to study the effect of insulin on non-protein nitrogen compounds of blo Recently it has been demonstrated th insulin causes a decrease in the amino a nitrogen of blood; also, that the decrea in the amino acid nitrogen of the whole bo is entirely accounted for by a correspondi increase in urea.

The authors' experiments were perform on dogs fasted for 24 to 48 hours. Two tab are given. The first shows the effect insulin on distribution of non-protein nitro in blood. The results show a decrease amino acid nitrogen, with a correspondin larger increase in urea nitrogen. Sokhey a Allan's results suggest that the increas excretion of nitrogen after insulin might due to a breakdown of protein for the sake glucose formation. This hypothesis wo suggest that the production of urea should increased in proportion to the fall of bl sugar, and to the length of time the hyp glycemia is maintained. To test this hypo esis, in three experiments shown in ta two, the blood sugar and the amino and u nitrogen were followed in whole blood f 7 to 9 hours. In two of these experime the urea not only showed no increase, b definitely decreased, contrary to the res obtained in the ten other experiments. Th results indicate that the formation of urea not dependent upon the level to which bl sugar falls, nor upon the duration of the hyp glycemia. The dosage of insulin like seems to have no influence on the amoun urea formed. The results suggest either t the low level of blood sugar is not itself stimulus which causes the increased cata ism of nitrogenous material, or possibly the nitrogenous reserve is limited in quan as otherwise prolonged hypoglycemia sho cause a greater increase in urea. It has b suggested that the extra nitrogen excret after insulin has its origin in a reserve "deposit protein" which may be depleted fasting. Possibly this reserve may be me the free amino acids of the tissues.

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Antirachitic Potency in Relation to Volume of Oil in the Liver of the Cod. — Alfred F. Hess, Charles E. Bills and Edna M. Honeywell. (*Journal of the American Medical Association*, **92** : 226, Jan. 19, 1929.)

The authors found that, contrary to current opinion, antirachitic potency varies inversely with the amount of oil in the liver of the cod. From extremely poor livers, oil was extracted which was 200 times more potent than high grade cod liver oil, and far more potent than any oil heretofore assayed. Oils from the livers of individual cod may vary 1,000 times in their antirachitic value.

Treatment of Diabetes Insipidus with Pituitary Posterior Lobe Extract Applied Infranasally. — John R. Campbell, Jr., and Herrman L. Blumgart. (*American Journal of the Medical Sciences*, **176** : 769, Dec., 1928.)

The authors studied 8 cases in succession of diabetes insipidus of various etiologies. Intranasal application of posterior lobe pituitary extract was as efficacious as hypodermic injection in controlling the fluid intake and urinary output. The authors draw attention to the importance of inserting the cotton pledget soaked with pituitary extract high in the nasopharynx.

Some Clinical Aspects of Hypothyroidism. — A. H. Gordon. (*Canadian Medical Association Journal*, **20** : 7, Jan., 1929.)

Gordon presents a group of cases having the common factor of diminished thyroid gland activity, but in their external appearances showing dissimilar clinical characters.

Perhaps the disease most commonly confounded with hypothyroidism is pernicious anemia. Chronic nephritis is the disease most likely to be mistaken for myxedema. Mental disturbances, especially of the depressed type, are sometimes associated with hypothyroidism. Pericarditis with effusion, secondary anemia, migraine and a case of on-coming cardiac pain and weakness have been observed and are reported.

When starvation, hypopituitarism and Addison's disease can be excluded, persistently low basal metabolic rates usually mean hypothyroidism, but in the present state of knowledge it is unwise to make this diagnosis on the basal rate alone. The consideration of myxedema raises a number of issues. Fahr describes a type of heart which he believes to be due to myxedema. He describes also a type of electrocardiogram associated with it. At any rate a damaged heart in myxedema may hold its own with the low basal rate and consequently lessened work, but with thyroid medication, which acts in the same manner as exercise, the inefficient organ may reveal its inefficiency by giving rise to symptoms. It is necessary, therefore, to proceed with great care in thyroid therapy when any evidence of cardiac damage exists. It is in the lesser grades of hypothyroidism that symptomatology becomes vague and diffuse. Dysmenorrhea in young women, recurrent colds with asthenia, fleeting pains, and many other conditions, have been attributed to hypothyroidism. The pathology of hypothyroidism is essentially the story of the degeneration of the thyroid gland, which many now regard as a sequel of adolescent goiter. Usually the damage is permanent and treatment is for years or forever.

Two methods of treatment are the massive and the gradual. In the former there is given a dose of gland substance calculated to raise the lowered basal rate to normal as rapidly as may be; the other is a slower method with fractional dosage. Having in mind the cardiac dangers resulting from a suddenly elevated basal rate, one should consider the gradual method in subjects of vascular damage and those in the later ages, but in all instances, with the commencement of thyroid therapy, rest should be advised. Thyroxin, as a substitute for thyroid substance, may be given in the proportion of 0.3 mgm. for each unit of lowered basal rate, but reaction to it is sometimes severe, and vomiting, collapse, generalized pains, and anginoid pains may result. Broadly speaking, 0.3 mgm. of thyroxin corresponds to 5 gr. of thyroid extract.

Gordon has never seen a case of hyperthyroidism restored to complete health, either by medicine or surgery, nor a case of hypothyroidism return to an absolute normal. However, miraculous results are achieved by appropriate therapy.

Effects of Substances Other than Carbohydrate in Relieving the Toxic Symptoms of Insulin. — Julius J. Selman and S. Frank Weinman. (*American Journal of the Medical Sciences*, **176** : 865, Dec., 1928.)

The authors offer a preliminary report of the effects of substances other than carbohydrate, administered orally to cases of

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diabetes mellitus with symptoms of insulin overdosage. Five of six of these patients showed complete and prompt symptomatic recovery. Four recovered following the administration of mineral oil and one following the oral administration of pure protein. The authors do not give any explanation of these results but are contemplating further work in the hope of discovering the mechanism involved.

An Electrocardiographic Study on 123 Cases of Diabetes Mellitus. — J. Hepburn and Duncan Graham. (*American Journal of the Medical Sciences*, **176** : 782, Dec., 1928.)

In a series of 123 diabetic patients 56 showed serious electrocardiographic abnormalities at the beginning of diabetic treatment and that in a very fair percentage the electrocardiograms returned to normal after the diabetic condition was controlled by treatment.

It would appear from these observations that in the cases in which the electrocardiograms returned to normal after the diabetic condition had been controlled that the abnormal electrocardiograms had resulted from the effect on the myocardium of the perverted metabolism present in diabetes mellitus. Whether this is a direct action on the myocardium or an indirect one resulting from disease of the coronary arteries, or both, is difficult to answer. If one considers first the possibility of a direct effect on the myocardium, it may be stated that none of the few cases of severe acidosis studied showed an abnormal electrocardiogram and that many severe diabetics with hyperglycemia had normal electrocardiograms. As hyperglycemia and the products of the perverted metabolism present in diabetes mellitus apparently do not produce a direct effect on the myocardium resulting in an abnormal electrocardiogram, the possibility of an indirect effect from disease of the coronary arteries appears more likely.

In a discussion on the relationship of arteriosclerosis to diabetes mellitus, Joslin has clearly shown the effects of present methods of treatment of diabetes mellitus on the clinical course of this disease and has stressed the importance of the prevention and control of vascular disease in diabetes mellitus. In considering factors responsible for the development of vascular disease at an early age in diabetes mellitus, he has suggested the high percentage of fat in the diabetic diet as a cause. In the series of cases reported in this paper all the patients received diets containing the same percentage of fat. The results show that with the diet prescribed the normal electrocardiogram remained normal and the abnormal tends to improve.

When the vascular changes leading to death in diabetes are considered it is found that they are chiefly, if not wholly, confined to the intimal coat of the vessel, whether it be in the arteries of the heart, brain, kidney or lower extremity. Further, the early intimal changes are inflammatory in type, degenerative changes being secondary and appearing later. It is generally believed that no single factor is responsible for these changes in the intima. Yet there is general agreement that infection is the most important single cause. It may be that in diabetes mellitus the premature development of vascular changes is the result of infection acting in the presence of the abnormal metabolism of diabetes mellitus.

Insulin in Oily Suspension. — O. Leyton. (*Lancet*, **216** : 362, Feb. 16, 1929.)

More than a year ago Leyton came to the conclusion that some cases of diabetes mellitus with the usual typical thirst, polyuria, and hyperglycemia made a complete recovery provided they were treated with a fixed diet which supplied sufficient energy and tissue repairing protein along with insulin, in doses which kept the concentration of the sugar in the blood below 0.15% throughout the 24 hours. In order to obtain this control of sugar in the blood some cases might require four or more injections of insulin during the 24 hours which made the treatment difficult.

It occurred to Leyton that it might be possible to prolong the action of an injection of insulin by delaying its absorption and thereby obtain the desired effect. He had a manufacturer supply him with insulin in an oily suspension and has used it in his private and hospital practice. He can give 90 units as a single dose, which will control the sugar of the blood just as well as 3 aqueous doses of 30 units each at intervals of 6 hours.

Diabetes Albuminuricus or Chronic Nephrosis.—Albert A. Epstein. (*New York State Journal of Medicine*, **28**: 1335, Nov. 15, 1928.)

The first and foremost manifestation of nephrosis is an intense and persistent al-

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minuria. The proteins present in the urine in albuminuria have been found to be identical with the proteins of the blood. Albuminuria, according to Epstein, in so-called nephrosis represents an active excretion of the serum proteins by the kidneys. Because of a change in the proteins, be it chemical, physical or biological, as a result of which the body is unable to utilize them for whatever function proteins serve, they are excreted by the kidneys as foreign substances in the same manner that the kidneys excrete any other foreign matter present in, or introduced into, the blood stream. Just as in diabetes mellitus the glycosuria results from the perversion of carbohydrate metabolism, so in this disease the albuminuria has back of it a perversion in protein utilization. To this fundamental process Epstein has given the name "Diabetes Albuminuricus".

An increase in the fatty substances is practically a constant finding. One of these fatty substances, the cholesterol, was studied intensively. The cause of the hypercholesterolemia is uncertain although there is no doubt as to the relation of the cholesterol content of the blood to the activity of certain glands of internal secretion as the suprarenal and the thyroid.

The basic disturbance of diabetes albuminuricus is a subversion of protein metabolism. The albuminuria, the loss of protein substance from the blood, the edema, the lipoidemia, the reduced basal metabolism and other evidences of tissue starvation, all result from this basic disturbance. The problem in the treatment resolves itself into three specific propositions.

1. To replace the protein loss of the blood plasma. 2. To compel the tissues to utilize the protein and incidentally to reduce the lipoidemia. Thyroid often aids in attaining this desideratum. 3. To reestablish normal metabolism. When high protein feeding fails to accomplish this the institution of thyroid is definitely indicated. It is to be remembered that the main purpose in the use of thyroid is to stimulate protein utilization. It does not aim to replace protein feeding which is fundamental in the treatment of this disease. The amount of thyroid necessary to reestablish normal metabolic conditions in myxedema is relatively small, but in diabetes albuminuricus the amount of thyroid or thyroxin necessary to produce a therapeutic effect is most extraordinary. Daily doses of from 1.0 to 4.0 grams of thyroid are often required over long periods of time to elicit a metabolic response. While experience teaches that uncomplicated cases are susceptible of complete cure by the intelligent and persistent use of the high protein diet and thyroid therapy, it must be remembered that 6 months to 2 years may be necessary to accomplish this result. The presence of complications not only alters the outlook, but necessitates modifications of the therapeutic procedures.

Hyperthyroidism in Primary Hyperplastic Adenomatous and Colloid Goiters. — Hillier L. Baker. (*Illinois Medical Journal*, **55** : 111, Feb., 1929.)

The etiology of hyperthyroidism has been ascribed to many causes. Opinion at present seems to favor the view that in exophthalmic goiter the secretion is a perverted one, while in adenomatous and colloid goiter there is perhaps either an increase of thyroglobulin produced, or the thyroglobulin is not stored in the normal manner and the clinical entity described as hyperthyroidism is thus initiated.

In this series of cases of hyperthyroidism the exophthalmic or primary hyperplastic goiter made up 31% of the cases reported. The adenomatous goiter with hyperthyroidism made up fifty per cent. Colloid goiter with hyperthyroidism made up 18.7% of the cases reported. Of this number approximately 5% showed exophthalmos. Microscopically there is very little to distinguish the colloid goiter from the normal gland. It is the adenomatous goiter with hyperthyroidism which causes confusion as to the pathological classification of goiter; 40.5% of the cases reported in which exophthalmos was found were classified by the pathologist as adenoma. If, as Plummer believes, exophthalmos never occurs except in a gland showing hyperplasia and hypertrophy, these should be included in the exophthalmic group. There is a group of cases which show adenoma or an "adenomatosis" on re-operation. This finding has been present in several cases in which a primary hyperplasia was the finding at the first operation. The reason of adenomatous tissue in thyroid is not clear, but whatever the reason, adenomatous tissue is found in hyperplastic thyroids.

The incidence of hyperthyroidism in adenomatous goiter in this series of cases was most frequent during the ages of 21 to 40 years.

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The response to the use of iodin is similar in adenomatous and primary hyperplastic goiters and this factor raises a question as to their pathological difference.

The use of iodin, while beneficial causes an abeyance of hyperthyroid symptoms and does not result in cure. The improvement is temporary, and more apparent than real. The use of iodin should not replace the more safe and conservative polar ligations in severely toxic cases.

The Adrenal Factor in Hyperthyroidism. — G. W. Crile. (*Surgery, Gynecology and Obstetrics*, **48** : 371, Mar., 1929.)

The symptoms of hyperthyroidism are the same as the symptoms of adrenalism. The injection of adrenalin in a patient having hyperthyroidism produces an exaggeration of every symptom of hyperthyroidism. On the other hand, no amount of thyroid extract or of iodine can immediately cause any symptom of hyperthyroidism. Experimental evidence also confirms the clinical observation that as the thyroid activity is increased, the effect of adrenalin on the organism is stepped up in a sort of mathematical ratio. One fact alone is sufficient to show that the production of adrenalism is dependent on the thyroid, namely, that in myxedema the injection of adrenalin has little or no effect. In the presence of thyroid deficiency, adrenalin loses its power, but it is also true that in the presence of adrenal deficiency there can be no hyperthyroidism. Therefore, the thyroid and the adrenal glands are each equally essential to the production of hyperthyroidism.

The chief, perhaps the only, causes of thyroid crises are those factors that cause an increased output of adrenalin. The factors which cause thyroid crises are the following: pain, emotional excitation, foreign proteins, asphyxia, inhalation anesthesia, hemorrhage, and the injection of adrenalin.

The great role of the nervous system is shown by the following facts:

1. In hyperthyroidism, physiological rest is one of the most effective forms of treatment. 2. In many cases the cause of the disease can be traced to excessive nervous strain. 3. Ligation of the superior thyroid artery, which produces a break in the innervation of the thyroid gland, profoundly modifies the disease and usually converts a hyperplastic gland into a resting gland. To these should be added the following biologic facts: 1. That the disease occurs only in members of the human race, the principal characteristic of which is the development of the nervous system — especially of the brain. 2. That among the human race hyperthyroidism rarely occurs in the inferior peoples or in the stupid and criminal classes of the white race. All these facts indicate that the nervous factor belongs to the picture almost as definitely and potently as do the adrenal and the thyroid factors. The three dominant factors in the production of hyperthyroidism, therefore, are the thyroid gland, the adrenal glands and the nervous system.

The thyroid hormone causes a specific increase in the permeability of all the cells, hence an increased activity of the trillions of cells of the body. An important consequence of this specific action of the thyroid gland is an increase in the electric potential and in the electric conductivity of the tissues. Increased electric potential determines the range of the functional power of the organs and tissues. In myxedema both the conductivity and the potential of the tissues are exceptionally low — a fact in harmony with the clinical observation of the stupor and low metabolism of myxedematous patients — the opposite state to that in hyperthyroidism.

The thyroid cannot discharge the cells or the organs and tissues, the potential of which it builds up. The human, however, has a marvelous discharge mechanism which is entirely separate from the thyroid gland — the discharging mechanism is the nerve-adrenal combination. The active work — excessive work in hyperthyroidism — is due to the action of the nerve-adrenal mechanism. The thyroid mechanism is the charge-up mechanism; the adrenal-nerve mechanism the discharge or work mechanism.

Thus, to recapitulate: 1. Nervous excitation is known to be a cause of many cases of hyperthyroidism. 2. Relief from nervous strain leads to relief of symptoms and the return of the hyperplastic gland to the normal. 3. In cases of hyperthyroidism the division of the nerve supply of the thyroid causes great improvement, sometimes even complete disappearance of symptoms, and the return of the hyperplastic gland to the normal. 4. Every one of the known excitants of hyperthyroidism, namely, infectious diseases, focal infections, emotional excitation, etc., involves nerve excitation which in turn pro-

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duces an increased output of adrenalin. The adrenalin, in turn, has the power of activating the thyroid. In view of the above considerations it would appear that a primary adrenalectomy would have both immediate and remote advantages in cases of extreme hyperthyroidism.

Crile says that when one considers the correlation of the thyroid, the adrenals, and the nervous system it becomes clear that a new name must be given to the disease which has formerly been associated only with the thyroid by the term hyperthyroidism.

The Parathyroid Glands. — E. Larson. (*Clinical Medicine*, **36** : 170, Mar., 1929.)

From experimental and clinical evidence gathered by Larson, it would seem that the parathyroids are concerned in the maintenance of the normal level of the blood calcium.

That the parathyroids are concerned in detoxification of toxins absorbed from the gastro-intestinal tract has been a thesis supported by Dragstedt et al.

Medication in parathyroid deficiency may be of two types; treatment with calcium lactate, with lactose to increase absorption; and by the administration of parathyroid extract. The danger of overdosage with parathyroid extract should always be considered. Parathormone, subcutaneously, has proven beneficial in several cases. Snell treated a case of tetany, which did not respond to calcium lactate, with parathyroid extract and had favorable results. Hjort, in his report, stated that large doses of calcium lactate (5 gm. every 4 hours, day and night) were not very effective. Desiccated parathyroid substance was given in large doses (3 gm. daily — 166 times the ordinary dose) without any favorable influence. When parathyroid extract, 20 to 30 units daily, was administered parenterally, supplemented by oral thyroid therapy, a favorable influence was exerted. Several other cases treated by parathyroid extract have been reported. Replacement therapy by oral administration of either the fresh or desiccated glands has been of no avail, either experimentally or clinically. Desiccated parathyroid has been omitted from "New and Non-Official Remedies".

Allen, Compere and Austin found parathyroid therapy beneficial in the control of prolonged menstrual bleeding. Ogawa believes that it is helpful in promoting the calcification of fractures. Ross has demonstrated that removal of 3 of the 4 parathyroids definitely delays the union of fractures.

Repeated injections of parathyroid extract may lead to other disturbances than those produced by the hypercalcemia. Hueper has shown that they may lead to necroses in the myocardium, and in the cortex of the adrenal gland.

Pregnancy Complicating Simple Goiter and Graves' Disease. — H. Gardiner-Hill. (*Lancet*, **216** : 120, Jan. 19, 1929.)

Gardiner-Hill discusses the incidence, results and effects of pregnancy in simple goiter and Graves' disease from data obtained from a study of the histories of 115 married women suffering from these conditions.

Twenty-six were cases of simple goiter and 89 of Graves' disease. Of the latter, 71 may be classified as primary Graves' disease—patients in whom symptoms of intoxication had been present from the outset. The remaining 18 were cases of secondary Graves' disease in whom symptoms of intoxication had appeared after some years during which a simple goiter had been present. All but 2 of the 26 cases of simple goiter were sporadic. Twelve of these had originated primarily in adolescence and persisted into adult life, while the remaining 14 had developed in adult life. In all but two of this latter group the goiter developed originally during pregnancy or the puerperium. It would seem, therefore, that simple goiter, developing in adult married women at times other than these, is comparatively rare. In the majority of the cases the effect of pregnancy on the goiter was a further hypertrophy of the gland, and in multiparae the steplike enlargement which was found by Lawson Tait. In 2 patients on whom a partial thyroidectomy had been performed before pregnancy occurred there was a recurrence of the goiter during pregnancy. These patients also almost invariably developed symptoms of hypothyroidism in later life.

Of the 14 patients who had developed goiter in adult life, 6 had no subsequent pregnancy. Thyroid deficiency is often accompanied by sterility which can be overcome in a certain proportion of cases by treatment with thyroid extract. A considerable degree of thyroid deficiency was present in the majority of the cases after their first pregnancy and it appeared they had not received adequate treatment with thyroid extract. The development of goiter during pregnancy

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did not appear to have any harmful effect on pregnancy. The effect of pregnancy on the goiter was in nearly every case the same — i. e., a further hypertrophy of the gland. In later years the majority of these individuals developed well-marked symptoms of hypothyroidism.

In 8 of the 71 cases of primary Graves' disease the disease originally developed during pregnancy. In 6 this had no adverse effect on the pregnancy. In the seventh patient, although the pregnancy was carried to full term, the child was stillborn. The eighth patient miscarried at 3 months, very shortly after the onset of the disease. It may be concluded that primary Graves' disease developing during pregnancy in the majority of cases does not materially affect the course of the pregnancy.

The incidence of pregnancy in secondary Graves' disease was low, only 2 instances occurring out of 9 cases in which it was possible.

In the series of cases of primary Graves' disease the incidence of pregnancy was 50% of the possible cases.

In cases of Graves' disease the poor results of pregnancy — miscarriage or premature birth in 50% — may be attributed to shocks, mental stress, and inadequate rest and treatment, for where satisfactory conditions were attained and mental stress was absent the results were generally good. In the cases which relapsed after pregnancy there was more often than not a history of miscarriage or premature birth. On the other hand, when the pregnancy was carried to a successful termination, the improvement in the symptoms was generally maintained.

Hyperthyroidism Induced by Synthetic Thyroxin in a Patient Affected with a Pluriglandular Syndrome with Scleroderma and Cataract. — P. Sainton and H. Mamou. (*Presse méd.*, **36** : 8, 1928.)

Presentation of a patient who gave manifestations of thyro-testicular insufficiency. The patient was treated with thyroid and parathyroid preparations, with injections of hypertonic saline solution and finally with subcutaneous injections of synthetic thyroxin. Following one injection of only 5 milligrams the syndrome of hyperthyroidism made its appearance: tachycardia, tremors, psychic hyperexcitability, loss of almost 2 kgms. of body weight within 2 weeks, without glycosuria. These conditions correspond entirely to the symptoms called forth by the injection of organic thyroid extract. Great caution is, accordingly, enjoined with the use of thyroxin subcutaneously.

The Role Played by Disturbances of the Sympathetic Nervous System and of the Endocrine Glands in the Pathogenesis of Cutaneous Affections. — A. Lévy-Franckel and E. Juster. (*Urol. and Cutan. Rev.*, **30** : 327, June, 1926.)

Studies of the sympathetic nervous system have shown the possibility of perceiving the disturbances of the functioning of the nervous system in its regulatory effect upon the epidermis. Outside of its own proper action upon the cell and upon the cutaneous glands the sympathetic system acts by its role as regulator of the circulatory system. The importance of the circulatory factor begins to come more and more into evidence. Another source of cutaneous impulse is the humoral impulse and particularly the hormonal. The blood which irrigates the skin contains the products of the glands of the economy, and notably of the endocrine glands, the action of which upon the morphology and the growth of the body is considerable.

The researches of endocrinologists have revealed numerous examples of the relationship existing between skin troubles and lesions of the endocrine glands. In like manner the clinical examination and laboratory tests — mainly basal metabolism — have made possible the demonstration of this hormone action in numerous cases of trophic cutaneous diseases. Also, the specific activity of the cells of the skin and of the cells of the cutaneous glands aside from all nervous or humoral action must be taken into account. Guillaume assigns to the cutaneous covering, considered as an organ, an antitoxic role in close correlation with the glands of internal secretion. Thus without wishing to make of the skin an endocrine gland it should be considered as susceptible of its own proper reactions corresponding with the particular status of its cells and of its glands. An analysis of the causes which regulate the proper functioning of the epidermis, of the epidermic products and of the cutaneous glands shows that these causes are the same as those which regulate the secretions in general.

The authors studied exhaustively certain cutaneous affections in regard to their rela-

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tionship with the endocrine sympathetic systems. In this group are the affections in which the role of the sympathetic and of the endocrine glands rests upon physiological bases. In most of these affections it is difficult to separate from a purely clinical point of view the action of the organo-vegetative system from that of the endocrine glands, and still more difficult to separate those due to the action of the sympathetic and those in which the dominant appears to be due to the para-sympathetic. Alopecia areata is among the affections with which the dermatologists see the connection with the endocrine-sympathetic. In the syndrome of the complete section of the peripheral nerves, hypotrichosis may vary from slight epilation to complete falling out of the hair. In hypertrichosis the role of the sympathetic nervous system and of the endocrine glands in the physio-pathology of hypertrichosis has been less disputed than the action of these two systems in the reverse phenomenon.

The role of the nervous system in the pathogenesis of hypertrichosis is all the more manifest since it is clearly demonstrated by physiology and the clinic. The part played by the sympathetic remains more obscure.

Pigmentary troubles may manifest themselves in the hair or in the skin. The influence of the nervous system upon the development of the nails is well recognized. The action of the nervous system and of the endocrine-sympathetic manifests itself equally in corneous patches. According to some authorities ichthyosis is of endocrine origin. Pilary keratosis, the authors have observed, accompanies a perturbation of the sympathetico-circulatory system (as in infantile paralysis). It may be under the dependence of a lesion of the endocrine system and in particular of the synergistic groups, the thyroid and the sexual glands. Seborrhea which seems to the authors to be more under the influence of the sympathetic nervous system and of humoral troubles (in the wide meaning of the word) than microbian infection, may be connected with an alteration of the endocrine system. Among the staphylococcic affections, a place quite apart should be reserved for acne. It is certain that the condition of the serum plays a role in its occurrence. Its frequency in women at the two extremes of sexual life suffice to prove this. The connection of acne with puberty and the menopause and the augmentation of basal metabolism in acne patients should suggest opotherapy in this affection. Kraurosis should be listed under the neuroglandular dermatoses. Pautrier admits the existence of an endocrine trouble as the origin of erythromelia. Bloch and Blamoutier have succeeded in obtaining notable amelioration in one case with polyglandular opotherapy.

The study of sympathetic reflex in adults affected with exfoliative marginal glossitis has shown the authors that there exist disturbances in the endocrine glands such as modifications of the pilometer and oculocardiac reflexes. The connections of limited desquamation with the sex-life of a woman, its frequence during the period of infancy corresponding with the development of the thymus, are interesting to notice. Milian and Perrin have made certain of the sympathetic pathogenesis of true dyshidrosis, not including dyshidrosiform epidermomycoses. The authors have twice observed that the occurrence of dyshidrosis coincided with a zone. In one of these two patients they discovered pilometer reflex disturbances. Raynaud's disease or symmetrical gangrene of the extremities is regarded as a sympathetic syndrome caused by the excitation of the vasoconstrictor nerves whatever the reason (exogenic, endogenic or endocrine) of the excitation. Erythromelalgia (Weir-Mitchell's disease) is a painful syndrome characterized by painful paroxysms. It is localized in the extremities, and is accompanied by redness, swelling of the integument, and local elevation of temperature. As in Raynaud's disease it is a vasomotor affection. Both are caused by an organic or functional perturbation of the medullary vasomotor centers. The endocrine dysfunction, particularly of the ovary adds an important factor in certain cases. Acrocyanosis of the hands of Brocq had been attributed by Marañon to an affection of the endocrine system (the hypogenital hand). In certain cases observed by the authors this influence was undeniable.

Psoriasis, eczema, urticaria, prurigos, pemphigus and pityriasis rubra pilaris come under the affections in which the role of the sympathetic nervous system and of the endocrine glands is based entirely upon therapeutic results.

The role of the sympathetic and of the endocrine glands rests only upon hypotheses in cases of naevi, Recklinghausen's disease, pruritus and lichen, erythrodermia and purpuras.

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Diabetes with Renal Glycosuria. — C. Voight. (*Lancet*, **213** : 916, Oct. 29, 1927.)

Among cases of true diabetes it is not unusual to notice certain ones in which the sugar tends to appear in the urine at either a high or a low level of blood-sugar concentration. Voigt reports an interesting case which illustrates the danger of an unrecognized low renal threshold to the successful control of diabetes by means of insulin.

In this case there is evidence that carbohydrates are not hurried through a rapidly emptying stomach; on the other hand, many processes in the gut will be modified by the want of the normal stimulus of acid leaving the stomach. It may be instructive to make gastric analyses in available cases of renal glycosuria, and to investigate renal threshold points of patients showing total achlorhydria.

Diabetic Acidosis without Ketonuria or Ketonemia. — Abraham Rudy and Charles M. Levin. (*N. Y. State J. Med.*, **27** : 1240, Nov. 15, 1927.)

The authors present this case because as they say diabetes may be discovered for the first time in old people and can be dangerous, contrary to common belief that the disease is mild in old age; also, this is another case of diabetic acidosis without the presence of acetone bodies in the urine and blood.

This is an instructive case of diabetic acidosis from which several important conclusions may be deducted. It proves the importance of a routine urinalysis in the acute case seen at home by the general practitioner as well as in his chronic cases. A positive sugar certainly does not prove that diabetes was the cause of this condition, at the same time the negative acetone does not exclude an acidosis.

The combination of all the symptoms together with the laboratory findings, gives the diagnosis. This case, as well as all the other cases of diabetic acidosis without ketonuria or ketonemia and also the experimental work on the acetone bodies, point to the conclusion that the acetone bodies are not always the direct or the only cause of diabetic acidosis resp. coma. The problem of diabetic acidosis must still be considered unsolved.

The authors conclude their paper as follows:

"A case of diabetes mellitus and acidosis discovered for the first time in a woman seventy-two years of age is presented. The problem of a diabetic acidosis without acetone bodies in the urine and blood is discussed and literature reviewed. A typical diabetic acidosis and its treatment at home are described.

The chemical methods used in making determinations were the following.

For

1. Sugar in the urine, the qualitative Benedict test.
2. Acetone and aceto-acetic acid in the urine, the qualitative Rothera test (a nitroprusside test).
3. Plasma sugar, the Benedict method.
4. Aceto-acetic acid and acetone in the plasma, the Wishart application of the Rothera test to the plasma.
5. CO_2-combining power of the plasma, the Van Slyke method.
6. Quantitative blood urea, Van Slyke and Cullen's modifications of Marshall's method.

The Rothera test is the most delicate test for diacetic acid and acetone. It is sensitive to one part of aceto-acetic acid in 20,000 while ferric chlorid reacts only to about one part in 8000.

Clinical Recognition of Pituitary Tumors. — Oskar Hirsch. (*Lancet*, 212 : 1339, June 25, 1927.)

Hirsch describes the ocular type of pituitary tumor and bases his observations upon about 100 cases of verified hypophyseal tumors upon which he has operated. A characteristic symptom is the visual disturbance without any striking constitutional disturbance. However, the patients nearly always suffer from some disorder of the function of the genital glands.

Thyroid and Parathyroid Bone Tumors without Primary Lesion of the Thyroid Gland. — R. Alessandri. (*Surg., Gynec. & Obstet.*, **45** : 35, July, 1927.)

Alessandri writes of the difficulties encountered when endeavoring to make a sure diagnosis between a simple goiter and a benign tumor. He studies the possibility of metastases in benign lesions of the thyroid gland (goiter and simple adenoma). In a recent paper he demonstrated that several cases which were reported as bone endothelioma were really secondary tumors of thyroid (of suprarenal) type, often with seemingly benign primary lesions of the gland. Many hypotheses have been advanced to explain this behavior which does not conform to the

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cepted doctrines of the pathology of malignant as compared with benign tumors and with the simple hyperplastic or degenerative lesions such as the so-called goiter.

The theory accepted with most favor is that which seeks to prove the possibility of embryonal aberrations and of the formation of foci of thyroid tissue in abnormal sites. These at a certain time of life, generally more or less late, can give place to structures with a progressive development of neoplastic type. It must also be taken into account that tumors may develop in accessory thyroids and metastasize, because the primary tumor can be easily overlooked and the thyroid gland in its normal site shows no enlargement. Accessory thyroid is to be found in the neck, at the base of the tongue, and in the mediastinum. The last two localizations are the most important as thyroid so placed is apt to be overlooked at a routine examination. There are cases in which no change of the thyroid gland is present, not the slightest enlargement. Alessandri has observed and operated on two such cases. He reports them because the thyroid gland did not show even the slightest change or enlargement before the onset of the skeletal growth, during its development, nor after the operations, which in both cases had to be repeated because of recurrences. Nothing which could possibly represent the primary site of an eventual tumor whence the metastases might have proceeded could be detected in the regions of the neck, of the tongue, or in the mediastinum where aberrant thyroid glands are usually found.

Persistent Thymus. — W. L. Denney. (*Can. Med. Assn. J.*, **17** : 89, Jan., 1927.)

A case is reported of an infant, aged 2 months, who was having attacks of cyanosis with difficult respiration. This difficulty was apparently neither of the pure inspiratory nor expiratory type but occurred in either phase. At each attack death seemed imminent. No history was obtainable. The temperature was normal and respirations normal between attacks. The infant was emaciated but not acutely ill. A diagnosis of enlarged thymus gland was made.

Five days after admission a Roentgen ray treatment was given. This gave immediate relief. Eleven days after the first treatment the child had one slight attack of cyanosis. One other treatment has been given and now at the expiration of four days there have been no attacks. The general nutrition of the child has improved and the weight increased.

The Carbohydrate Metabolism of Adrenalectomized Rats and Mice. — Carl F. Cori and Gerty T. Cori. (*J. Biol. Chem.*, **74** : 473, Sept., 1927.)

When rats surviving double adrenalectomy were subjected to a 24 hour fast, the liver glycogen disappeared and the blood sugar fell considerably below normal. In contrast to the liver glycogen, the glycogen content of the muscles of these animals remained the same as that of normal control rats fasted for the same length of time. The low blood sugar is linked with the lack of liver glycogen, since the muscle glycogen does not participate in blood sugar regulation. The absence of liver glycogen in fasting adrenalectomized rats is not the result of a disturbance in the synthesis of sugar into glycogen, since liver glycogen is formed at a normal rate when glucose is fed. Twenty-four hour fasting adrenalectomized rats absorbed glucose at a much slower rate than twenty-four hour fasting normal rats.

During 4 hours of glucose absorption the adrenalectomized rats without insulin oxidized 373 mg. of glucose and formed 270 mg. of glycogen (124 mg. in the liver and 146 mg. in the rest of the body). The adrenalectomized rats receiving insulin injections oxidized 471 mg. of glucose and deposited 37 mg. of glycogen in the liver and 185 mg. of glycogen in the rest of the body. The difference in liver glycogen of 87 mg. corresponds closely to the difference in glucose oxidation of 98 mg., while the glycogen deposition in the rest of the body (chiefly muscles) is not materially changed. The same results have been obtained previously on rats with intact adrenals, where a discharge of epinephrin in sufficient amounts to produce a metabolic effect could not be excluded. Since the adrenals were absent in these experiments, the conclusion has been drawn that the lessened deposition of liver glycogen and the increased sugar oxidation, also to be observed in insulinized rats with intact adrenals, are due to insulin alone and not to a combined action of insulin plus epinephrin.

Previous experiments have shown that insulin injections lead to a decrease in the liver glycogen of fasting insulinized mice. An identical result has been obtained on mice from which both adrenals had been removed 20

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to 30 days previously. The adrenalectomized mice without insulin showed 2.16% liver glycogen after a fasting period of 1 to 5 hours. The adrenalectomized and insulinized mice that were killed simultaneously showed only 0.79% liver glycogen. Since the effect of insulin on the liver glycogen of fasting animals is the same, whether or not the adrenals are present, there is no need to assume that epinephrin is responsible for the decrease in liver glycogen following insulin injections.

Action of Epinephrin upon the Cardiac Rhythm. — Harold L. Otto. (*J. Lab. and Clin. Med.*, **13** : 70, Oct., 1927.)

Since epinephrin by virtue of the powerful accelerator stimulation it induces can cause the appearance of cardiac arrhythmia, in many instances of a dangerous or unpleasant nature, it is distinctly advisable to administer it with caution particularly to cardiac patients or those individuals presenting a history of having had one of the cardiac arrhythmias.

Exophthalmic Goiter

(*Continued from page 10*)

"Eponymically, Parry's disease — and not Basedow's or Graves' disease — is the most appropriate designation for both toxic adenoma and exophthalmic goiter, for Parry was the first observer who described all varieties of toxic goiter.

"Clinically, a nodular goiter without exophthalmos may be as toxic or even more toxic than a smooth, diffusely enlarged, or exophthalmic goiter with pronounced ocular signs. The prognosis in a severe case of toxic adenoma with myocardial insufficiency is much graver than that in a moderately severe case of classic exophthalmic goiter in which the patient has markedly bulging eyes and a fairly intact myocardium.

"Although toxic adenoma may run as severe a course as exophthalmic goiter, its clinical manifestations are usually milder, and the surgical results are more satisfactory than in classic exophthalmic goiter.

"The more favorable surgical results in toxic adenoma are due not to any fundamental difference in nature from exophthalmic goiter but to a variation of a single disease: In exophthalmic goiter, generally the entire gland is diffusely involved in the pathologic process, while in toxic adenoma of the thyroid the gland shows one or several pathologic foci with intervening healthy tissue between the affected areas. Hence, generally, the symptoms are milder, and the surgical resection is more satisfactory than in exophthalmic goiter."

The existence of toxic adenoma as a separate disease entity can not at present be conclusively established. In view of the widespread references in the literature, however, and the constant reference to it in relation to exophthalmic goiter, it is well to consider the opinions of those who have most thoroughly studied it.

(*To be continued*)

1. Ginsburg, S., *Arch. Int. Med.*, 1929, xliv, 73.
2. Mayo, C. H., and Plummer, H. S., "The Thyroid Gland." Beaumont Foundation Lectures, Series 4, Mosby Co., St. Louis, 1926.

Obesity. — Maximilian Kern. (*Clin. Med. and Surg.*, **34** : 440, June, 1927.)

The present-day classification of obesity is as confusing as it is unsatisfactory. In most cases it is too broad to meet all requirements. The endocrine factor is not properly understood, and therefore is underestimated. On the other hand, basal metabolic readings are not a sufficient guide in the proper management of nutritional disturbances.

No matter how caused, obesity, in a medical sense, is generally a manifestation of pathologic condition and just as much a disease as is cancer or any other condition which expresses itself in abnormal tissue growth. There are exceptional individuals who, though obese by definition are still not pathologic subjects. Climatic conditions, food used, and their general mode of living may affect the definition when applied to them. Brown and Keith have observed that the circulating blood and plasma volume, when compared with body weight, is less in obese than in normal persons. As a rule fat deposits are more abundant in regions where the circulation is poor. Strouse and his associates have shown that the obese tend

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store rather than to burn fats derived from carbohydrates. There is also a discrepancy in the metabolism of proteins between obese and normal persons. There must be some constitutional factor — some diathesis or temperament-affecting metabolism and obesity, as it is known that the latter is not always the expression of a disproportion between the food intake and bodily expenditure. Grafe considers that in every case of obesity from overeating there is a constitutional factor involved and that the attempt to define two types of obesity does not conform to facts.

Obesity, either generalized or localized, is a well-marked part of the clinical picture observed in disturbance of the secretions of the thyroid, pituitary, gonads and suprarenals. Obesity is a predisposing or direct cause of diabetes, arterio-sclerosis, arterial hypertension, and cardio-renal disease. The medico-actuarial statistical tables show that every pound of fat above normal for age and height is reflected in a regular increase in the mortality rate; the most favorable rate, in fact, not being in those which show normal weights but in those whose weight is substandard.

Prepubertal obesity in children, when pathologic, may be a precursor of imperfectly developed sex characters and organs. Marañon recommends that obesity in children, with metabolism of five per cent below normal, should be treated by thyroid extract, and by ovarian extract in the case of girls. The treatment of obesity can at no time be carried out along specific lines, and may frequently be a hazardous undertaking. Without the proper consideration of all the factors involved, such as nutritional irregularities, endocrine disturbances, heredity and habits it may not only be unsuccessful but in many cases harmful. The most important changes arising from too rapid reduction of fat tissue are excessive production of fatty acids and acidosis. In mild cases of obesity, a loss of from 3 to 6 pounds per month should suffice. In cases of excessive obesity with cardiac decompensation, up to 30 pounds a month can be reduced without danger if the patient is carefully supervised.

Diabetes Mellitus and Myxedema. — Heber C. Jamieson. (*Can. Med. Assn. J.*, **17** : 88, Jan., 1927.)

The occurrence of glycosuria in the myxedematous patient has been noted, though the number of cases of diabetes mellitus with myxedema reported have been few. Wright reports two. In one the basal metabolism was −26, and in the other −28. An interesting case is reported.

A man, aged 37 years, presented all the classical symptoms of myxedema. Thirteen years before seen by the author, he was passing an excessive amount of urine. He suffered a gradual increasing weakness though his appetite increased. About a year before Jamieson saw him he lost his hair. Six months later he noticed swelling of his eyes, and his eyelashes fell out. Basal metabolism was −35 and −36. There was neither sugar nor acetone in the urine. In view of his history he was placed on a diet low in carbohydrate. His blood sugar before breakfast was 0.120%. Thyroid extract, 1 grain three times daily, was given. As long as he was allowed to become myxedemic he remained free from symptoms of diabetes. When thyroid extract was given and the basal metabolism approached the normal, all the classical symptoms returned. An attempt was made to solve the difficulty by giving small doses of the extract and small doses of insulin, which resulted in improvement in his condition.

The Sensitizing Action of Alkalies. — A. Hemingway. (*J. Physiol.*, **62** : 81, Oct. 30, 1926.)

That the tone and activity of tissues containing plain muscle, such as blood vessels, intestine, uterus, etc., is largely dependent upon the acidity or the alkalinity of the fluids with which they are bathed has long been known. In addition to these changes in tone and activity there is considerable evidence that certain drugs are more effective when used in an alkaline medium. It has been observed that an exaggerated response to adrenalin accompanies the reaction to alkalies.

Pre-Operative Preparation of the Diabetic Patient, with a Discussion of the So-Called Diabetic Gangrene. — Edward H. Mason. (*Can. Med. Assn. J.*, **17** : 23, Jan., 1927.)

The well controlled diabetic is no more susceptible to infections leading to surgical complications than is the non-diabetic. Attention to details, minor details in the daily hygiene of the patient, however, should not be overlooked. Failure in this respect will

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lead to trouble. Prompt attention to small pimples and boils, cleanliness of the skin, and the daily hygiene of the feet, are measures concerning which instruction is due to every diabetic.

Most diabetics who develop surgical complications peculiar to their diabetic state fall into two classes: (1) young individuals who fail to live up to a strict dietetic regime, and (2) individuals beyond 50 years of age, who, either have a low grade diabetic condition of at least several years standing which has never been considered seriously, or patients who break their diet allowing themselves to have persistent hyperglycemia. Most major surgical complications including gangrene occur in patients of the first group of the second class, the most important complication being gangrene.

In most instances there is plenty of time to prepare a patient for operation but emergency cases occasionally are found. On the day of operation the patient should have a good fluid balance, some glycogen reserve, no ketosis, and an approximately normal blood sugar. Ten units of insulin given just before the operation is a wise procedure. The post-operative period is as important as the pre-operative. Freedom from glycosuria must be maintained if possible, and ketosis of any degree of severity prevented. This can be accomplished through diet, fluids and insulin. Vomiting once established dehydrates rapidly and will convert a mild ketosis into a severe one. The diet should be gauged according to the carbohydrate tolerance of the patient, giving fluids and soft food at the start. Milk as a sole food is not especially suitable for this period as it is relatively high in carbohydrate.

The major surgical complication of diabetes mellitus today is gangrene, almost always of the lower extremities. It usually develops in the untreated or poorly treated cases. Diabetic gangrene is now held to be due to arteriosclerotic changes. Insulin cannot change the arterial condition, but its control of blood sugar and local care will save many limbs. The quartz mercury vapor lamp is a valuable aid in these cases.

A System of Microscopic Tubules in the Thyroid Gland. — R. R. Fitzgerald. (*Can. Med. Assn. J.*, **17** : 542, May, 1927.)

Fitzgerald reports the results of his investigations which confirm the presence of a system of microscopic tubules in secreting epithelia and found in the thyroid gland. The microscopic tubules were demonstrated in normal thyroid tissue obtained at autopsy and pathological material removed surgically. Tissue was prepared by the method described by Williamson and Pearse. When it is properly prepared by this method a new structure is seen in the epithelium.

The histological studies of Williamson and Pearse, extending and completing the work of previous investigators, seem to prove conclusively that two distinct secretory processes must be recognized in the normal thyroid gland. One is the relatively passive process resulting in the storage of colloid; the other is an active process resulting in the formation of a distinct product which is not colloid. Between these two separate phases there is an indifferent or resting phase. The appearance of the system of microcanaliculi varies in different parts of the normal gland according to the particular stage of physiological activity which happens to be present. In the colloid-storage phase they are drawn out to minute hair-like lines which are almost invisible. In the indifferent or resting phase they appear as thick black branching and communicating lines occupying a position near the center of the epithelial column. The resulting structures sometimes resemble giant mitotic figures. In the active secretory phase they appear as purple, almost transparent tubules filled with deeply chromatic coarse granules. The tissue of Graves' disease exhibits these structures in every vesicle. The so-called fetal adenomas, built of closely packed small vesicles, show well-developed microcapillary systems. In adenomas composed of colloid-containing tissue the microcanaliculi are absent, or are too fine to be detected by this method. The significance of this system of microtubules has not been established. Their association with the process of active secretion is constant and striking. They can only be demonstrated with great difficulty when the gland is in the stage of colloid storage, but they are constantly present, large, and contain granular material when the epithelium is in the stage of active secretion.

Bearing in mind the conspicuous presence of distended microcanaliculi in all active secreting tissue it seems logical to suggest that they may be channels of absorption in which secreted material is collected from the interior of the acinus, conveyed outward through

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the layer of epithelial cells, and delivered to the lymph spaces outside the vesicle. However, when the neoplastic states are examined well-developed canaliculi are found in tissue in which the other characteristic features of secretory activity are lacking. If these distended canaliculi are the result of stagnation and passive distension by secretion unable to escape in the ordinary way on account of encapsulation, this observation would tend to detract from the theory that the microcanaliculi act as absorption channels for secreted substances.

Studies on the Action of Parathormone. — Wilhelm C. Hueper. (*Ill. Med. J.*, **52** : 393, Nov., 1927.)

Hueper examined the effects produced by the injection of excessive amounts of parathyroid extract on the organs of dogs. The clinical course observed in the animals did not differ in general from the description given by Collip. Study of the causes of the reported pathological alterations has to be based upon the knowledge of the physiological effects of the parathyroid hormone. Regulating the calcium metabolism it controls the acid-base balance of the cells and the body fluids and also the equilibrium of the tonus of the vegetative nervous system.

The parathyroid extract administered in physiological doses induces:

1. A prolongation of the systole and a shortening of the diastole of the heart through irritation of the pneumogastric nerve.
2. A dilation of the vessels of the internal organs.
3. An intensification of the tonus of the stomach and the intestine.
4. A rise in the calcium level of the blood.

Excessive amounts of the parathyroid extract produce by an exaggeration of the above noted effects:

1. A gradually increasing incompleteness of the diastole of the heart and a slow and irregular pulse resulting in a drop of the blood pressure and an impairment of the general circulation.
2. They induce an excessive intensification of the tonus of the stomach and intestine, causing vomiting and diarrhea.
3. They augment by the highly increased blood calcium the coagulability of the blood to such a degree that the formation of thrombi in the congested vessels becomes imminent.
4. They cause such a supersaturation of the blood with lime salts that these are precipitated in various organs interfering eventually with their proper functioning.

Injections of parathyroid extract administered in larger amounts and short intervals should not be given for therapeutic purposes without a continuous control of the blood calcium, because excessive doses of this hormone produce dangerous circulatory disturbances and calcifications in vitally important organs. Even injections of larger doses in intervals of 3 to 4 days to avoid accumulative effects are not absolutely harmless. This has been proved by recent laboratory experiments.

Hueper, in order to study the influence of the parathyroid hormone upon the production and calcification of osteoid tissues, fractured one leg in cats. At the end of the third week the callus of the treated cats exceeded in amount and degree of calcification by about 20-30% that of the control cats. Histological examinations of the fractured bones showed also a higher amount of newly formed bone and a higher degree of consolidation than was present in the control cats. Hueper says if further investigation should substantiate his present findings he would consider parathyroid extract as an eventually useful therapeutic in cases of delayed fracture healing and in the treatment of rickets. He calls attention to the following:

Dogs which had received injections of parathyroid extract and in which the blood calcium level was raised to around 15 mg. showed a markedly increased production of urine. The results of the investigations including histological examinations and findings and considering that the parathyroid hormone is a strong stimulant of the vagus nerve a beneficiary effect of this hormone in cases of oliguria or anuria, being the result of an acute glomerulonephritis or reflex anuria, is very likely. By relieving the vessels of the kidney from the excessive vasoconstrictory splanchincus tonus the hormone will effect the reëstablishment of a proper circulation and the subsequent secretion of urine and excretion of the retained waste products. Moreover, it will raise the blood calcium level which is frequently found to be low in glomerulonephritis and thereby arrest the irritability of the muscles. The regulating effect of the parathyroid hormone upon the activity of the heart may be mentioned too in this connection.

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A Case of Mongolian Idiocy, Occurring in One of Male Twins. — Gordon Chown. (*Can. Med. Assn. J.*, **17** : 943, Aug., 1927.)

A case is reported which supports the views of McLean, Halbertsma, Strauch, Mitchell and Downing that where Mongolism occurs in twins, it is the result of a double ovum pregnancy, and that the etiology is due to a defective germ plasma.

Herrman, while supporting this theory, goes further and states that Mongolism is a reversion to a primitive type, or in other words it depends upon the reappearance of recessive unit factors. The former view that the condition is due to exhaustion products: physical or nervous strain, syphilis, alcoholism, consanguinity, conditions operative during pregnancy, and endocrine imbalance, seems now to be refuted.

Xanthoma Diabeticorum: An Unusual Process of Involution. — Eli Goldstein and John Harris. (*Am. J. Med. Sc.*, **173** : 195, Feb., 1927.)

The authors describe an unusual case of xanthoma diabeticorum which showed a peculiar process of involution not mentioned in the literature. This occurred in a patient suffering from diabetes mellitus, to whom insulin was administered in the late stages of the disease. The consensus of opinion in the literature reviewed is that when the xanthoma nodules undergo resolution, they disappear completely or at the most leave a pigmented area over the site of the lesion. In the case here described three types of resolution went on simultaneously with little or no reference to the general condition: (a) the lesions on the palms disappeared completely; (b) those on the elbows coalesced and left large pigmented patches; (c) those on the legs and thigh underwent degenerative changes resulting in extensive scar formation — a process hitherto undescribed.

The Laryngeal Nerves: Their Relation to the Thyroid Gland. — Homer Dupuy. (*So. Med. J.*, **20** : 15, Jan., 1927.)

The author says "The thyroid problem is with us, and laryngology must be given the opportunity of enlightening the profession as to the pre-operative and post-operative status of the larynx." He says that this is necessary in order to know whether this organ is damaged by pre-operative pathologic changes in the thyroid.

Observations Based on 173 Consecutive Goiter Cases. — S. O. Black. (*Internat. J. Med. and Surg.*, **39** : 28, Jan., 1926.)

There are four varieties of congenital goiter: vascular, colloid, cystic, parenchymatous. The last mentioned is the most frequent; the cystic the least frequent, but when present may rival in size the fetal head. The colloid is very rare.

The vascular enlargement is not a true goiter. It results as a rule from the long labor incident to face presentation, and usually disappears within a few days after birth. The parenchymatous enlargement, if of a size sufficient to induce pressure, may cause the child to be dyspneic at birth, with cyanotic facies, periodic unconsciousness and a crowing sound on inspiration. This type of goiter will not occur provided the mother has a sufficient quantity of iodin during her parturient period.

The acquired goiter is more frequent than the congenital. It may be simple, toxic or malignant. The true cause of variation in thyroid function is not known. Many cases of hyperthyroidism date back to an acute tonsillitis. The gland is affected more frequently in the female than in the male. To every one soldier from the southeastern states there were 15 from the northwestern with simple goiter, according to statistics of the World War. Kimball proved that hyperplastic and hypertrophied thyroids during childhood and adolescence were due to a deficiency in iodin. Thyroid enlargements have been eradicated in the public schools of Zurich, Switzerland, by giving a small dose of sodium iodide to the affected child each Monday morning.

All normal thyroids contain at least one-tenth of 1% of iodin; hyperplasia ensues when the amount is less. Adenomatous goiters contain iodin greatly in excess of the normal content. During pregnancy if the iodin supply becomes impoverished, the thyroid begins to enlarge automatically. Many multipara date the onset of their goiter to one or the other of their parturient periods. Should the expectant mother fail to get iodin her child might be born without a functioning thyroid, a cretin being the result. Any expectant mother developing parenchymatous enlargement of the thyroid should be given iodin salts at regular stated intervals to prevent goitrous offspring. Many children born with too little iodin have fetal adenoma in their glands, and

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these are apt to grow into adenomatous goiters, to become toxic, or to become malignant.

Cannon and Mix write of the interrelated physiology between the thyroid and the adrenal. They say that the adrenal is the whip to the thyroid, that it spurs the thyroid to greater activities during periods of emergency. Both these glands affect, through their secretions, the pulse rate, the pulse-pressure, and the respiration. The adrenal also throws into the blood stream additional quantities of sugar, to enable, as Mix states, the runner to increase his speed or the fighter his strength. The thyroid gland acts as the carburetor to the human machine, and through it the physiological elixir flows. Any glandular or secretory disturbance which results in the alteration of the chemical composition of its finished product, immediately disturbs one or the other of its functions. Hyperthyroidism often constitutes a problem for the internist and the surgeon alike. Frequently its symptomatology is such as to confuse it with paroxysmal tachycardia, neurasthenia, pulmonary tuberculosis and organic heart disease. Cannon states that thyroid function depends upon sympathetic nerve impulses. Mastin believes that the improvement following the ligation operation is due to an interruption of these impulses. All goiters, excepting small colloid ones, are potentially dangerous and should be subjected to early operation. It has been found that in the hyperplastic toxic goiter the administration of iodin is as efficient as the ligation procedure.

Practical Therapeutics

(*Continued from page 15*)

Proceeding from the hypothesis that an antagonism exists between lactation and ovulation it was supposed that lactation acted on the ovary and the genital sphere through the medium of endocrine products secreted by the mammary cell. Robert Bell recommended the ingestion of mammary substance in treatment of menorrhagias and even of fibromas as early as 1894. Various reports have been published concerning the efficacy of mammary organotherapy. On the basis of his observations in a series of 30 cases of menorrhagia or dysmenorrhea, Charlton concluded that the effect on menstruation if it exists at all, is not constant. The author possesses an extensive experience with mammary organotherapy. In a series of 15 cases of metrorrhagia or menorrhagia, treated with mammary extract, he had durable results in 7 cases.

If mammary extracts do exert a genuine therapeutic effect, even if inconstant, it remains to determine by what mechanism. It may seem plausible at first sight that the mammary extract acts as antagonist of the ovary. This explanation does not appear probable to the author for histological and experimental reasons. In two experiments in which he injected mammary lipoids into female guinea-pigs he found ovaries of normal appearance upon examination. Charlton demonstrated even more precisely that the extracts have no effect on ovulation.

Certain authors have spoken of an action on the uterine vessels. It is evident that a substance does exist in mammary extract which is capable of acting on the tonus of any vessel whatever. This vascular effect is, however, too weak and transitory to explain the effect of the medicament. An action on the uterine fiber has also been thought of. Fedoroff has noted that mammary extracts activate involution post partum. Scott and Ott have spoken of a myokinetic action. Adler, Schiffmann and Vystavel have obtained an atrophy of the uterus following prolonged use of the extracts. Cavagnis noted an increase in tonus which F. Spirito verified. But here also the action is slight and scarcely permanent and the author is not quite certain that this would suffice to explain the therapeutic effects obtained.

It is possible that mammary extract acts by an effect exerted through the medium of the adrenals. Adler, Schiffmann, Vystavel and Manzi have always observed in the course of their experiments that injections of mammary extracts in addition to their action on the utero-ovarian apparatus, occasioned a considerable hypertrophy of the suprarenal cortex and medulla. Such suprarenal hypertrophies are, however, too frequent following injection of organ extracts, to permit of a conclusion.

It may also be questioned whether mammary extract does not act on the uterine mucosa. This is an opinion which Adler has maintained, because having obtained abortions by the action of mammary extracts, he interpreted them as consequent to a disturbance of the terrain of nidation. No histologic evidence has been forthcoming in support of this hypothesis, however, which seems to merit further research, in the author's opinion.

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Practical Application of Our Present Knowledge of Calcium Metabolism. — A. T. Cameron. (*Can. Med. Assn. J.*, **16** : 759, July, 1926.)

The studies of Mellanby, McCollum and his co-workers have led to the identification of a new vitamin, fat soluble D, which is present in especially large amount in cod liver oil (also one of the chief sources of vitamin A). Hess has fractionated the oil, and obtained a non-saponifiable fraction soluble in acetone which is a thousand times more active than the original oil, and which is quite free from vitamin A. Butter contains much less of the new vitamin than does cod liver oil, milk a sufficiency for prevention, but not for cure of rickets, while egg-yolk is fairly rich in it. Of animal tissues bone-marrow is stated to be especially rich in it. It is not elaborated in the germinating seed as are several of the other vitamins.

Rickets, characterized by an incorrect and deficient calcification of bone tissue, can be produced in the young growing animal either by deficiency of calcium, or of phosphate, or of vitamin D in the diet. In the presence of an ample amount of the vitamin much smaller amounts of calcium and phosphate are sufficient to prevent rickets than when there is only a small quantity of D present. It conserves these mineral constituents in the body. In rickets there is found low serum calcium along with somewhat low serum inorganic phosphate, or low phosphate with normal calcium. In the former case the rickets may be accompanied by tetany. In rickets also there tends to be a negative calcium and phosphorus balance, owing to a continued loss of these elements from the body. In the normal growing child, bone requirements demand a marked calcium and phosphorus retention. Any digestive derangement which may upset the acid-base equilibrium may possibly, by affecting absorption of calcium and phosphates, lead to rickets. Acidosis is a frequent if not invariable accompaniment, and since acetone bodies are absent, it may be attributed to a mineral derangement. Incorrect dietary of the mother is probably a large contributory factor in nurslings. Rickets can be cured by cod liver oil, and by ultraviolet light. Direct sunlight contains sufficient of the ultraviolet rays to prevent onset of rickets, though perhaps not so readily to effect a cure. Clover hay made by exposure to sunlight is active; made in the dark it is inactive.

The curative effects of the ultraviolet ra can be produced by directly raying the ch or by raying a large number of different co pounds and food mixtures which are sub quently fed. It seems extremely proba that the food-stuffs that can become activa all contain cholesterol or related ster Vitamin D is not cholesterol, but it is pro ably a related sterol. The rayed substan retains its antirachitic potency for seve months, but apparently over-raying ag changes it to an inactive modificatio Roentgen rays and radium will not activa substances chemically related to vitam D, and will not cure rickets.

One variant of rickets is accompanied b tetany, or latent tetany. Tetany occurs i the following conditions: rickets with tetan infantile tetany of unknown origin; par thyroid deficiency through surgical or oth causes; excessive thyroid feeding in ra over-ventilation of the lungs; feeding o injection of sodium or potassium phosphat feeding or injection of large amounts of sodiu carbonate or bicarbonate, (and perhaps o other sodium salts); pyloric stenosis or sim lar conditions in which large amounts o hydrochloric acid are removed by vomiti or gastric lavage; occasionally in seve diarrhea; following injection of guanidin or methyl guanidine.

A normal degree of muscle and nerve exci ability depends upon a balance of certa ions; an increase of sodium, of potassium or of hydroxyl ions, and a decrease of calcium of magnesium, or of hydrogen ions leads to greater irritability. It would appear that in all of the above conditions that lead t tetany its onset can be satisfactorily explaine by a disturbance of the ionic ratio that go erns muscle-nerve irritability. Most infa tile tetanies, parathyroid insufficiency, a the tetany following sodium phosphate inje tion are definitely associated with a lower of the blood serum calcium concentratio The others seem largely due to an increase the hydroxyl ion concentration. Camer emphasizes the probability that these tetani result frequently from a combination of fa tors. He believes the tetany associated wi guanidine is a purely pharmacological effe not met in ordinary pathological conditio

Collip has shown that the concentrate product of the acid hydrolysis of parathyro glands, injected into animals in severe tetan following parathyroidectomy, quickly restor

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them to normal condition, at the same time raising their plasma calcium to normal level, and holding it there longer than the administration of calcium salts can do, whether these be given by mouth or injected. Such animals can be kept free from tetany for months, though, if injection of the extract be stopped, tetany recurs within a day or two. If the injection be given in large doses and at repeated short intervals the calcium of the blood is increased much above the normal level. When it is about twice normal other symptoms intervene, atonia, profound depression, anorexia, ataxia, vomiting, bloody stools, etc., and ultimately the animal dies. The same increased blood calcium, and ultimately fatal ending, follow injections of the extract into the normal animal. So far no antidote has been found for these effects from overdosage; evidently chemical control must at present be employed during the administration of the extract in clinical cases. These results have been confirmed by Macleod and others, including Moorhouse and Cameron. Cameron has showed that both the diffusible and the non-diffusible calcium are raised by this treatment — to approximately an equal extent — just as they are both lowered following parathyroidectomy.

Moorhouse and Cameron as a result of their studies with parathyroidectomized dogs have put forward a theory of the mechanism by which the blood calcium is maintained at a constant level. They believe that the parathyroids elaborate an internal secretion which controls the formation of a non-diffusible calcium compound in the blood, and that this, by a series of interlocked equilibria, keeps the diffusible calcium compounds of the blood to a constant ratio with itself. If the parathyroids function normally, the compound under their control will be kept at constant concentration and therefore the total blood calcium will remain constant. The slightly higher value for the plasma calcium of infant's blood suggests a more active parathyroid function. This theory, to be complete, must take into account the further control by vitamin D. While the administration of cod liver oil or of ultraviolet light restores blood calcium to normal in the rickety child with deficient blood calcium there is as yet no evidence to determine the nature of this control, though it seems to be closely interwoven with that of inorganic phosphate.

When calcium salts are given by mouth, or injected, it has been recognized for some time that there is merely a most transient effect on the height of blood calcium. Excessive doses produce only temporary benefit so it is easily understood why therapeutic doses can lead only to very transient results. The most that can be hoped for is continued slight benefit from moderate doses given at frequent intervals. The excess calcium may be, perhaps, in part secreted, but it would seem in large part to be deposited in the tissues, especially the bones.

Tuberculosis, rickets and various diseases have been associated with a disturbed calcium metabolism. However, accurate workers in tuberculosis seem to be agreed that no such disturbance is involved and that the administration of calcium salts is of no benefit. In epilepsy blood calcium is normal. This condition is not associated with parathyroid deficiency.

The types of parathyroid enlargement separately reported to accompany rickets in chickens, and to follow ultraviolet light treatment, merit attention, since, if such changes do occur, they tend to bring into alignment the actions of vitamin D and of the parathyroid secretion.

Diabetes: Reaction of the Diabetic Patient to Insulin. — Julius Jensen. (*Journal-Lancet*, **46** : 143, Apr. 1, 1926, and **46** : 170, Apr. 15, 1926.)

In this paper Jensen records observations in the treatment of about 200 cases of diabetes and glycosuria. Sugar-tolerance tests were extensively used in the investigation of the cases. He found them essential for diagnostic purposes and useful in illustrating the progress of the cases and thereby also giving an idea as to the prognosis. He thinks the best prognosis can be given in cases showing hardly any alteration of their sugar tolerance whilst under treatment; their diabetes seems to be of the stationary type that is not much influenced by any factors. A fairly favorable prognosis has been given in cases whose tolerance seems to show much improvement under treatment, but their condition is of a more fluctuating variety and therefore likely to fluctuate adversely when the patient is no longer under the care of the hospital. A distinctly unfavorable prognosis is of course given when the tolerance decreases in spite of treatment. Low sugar-tolerance curves were found on several occasions, often associated

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with hypoglycemia, and could almost always be explained by carbohydrate starvation in some form or other.

In order to obtain some experience of the immediate effects of insulin on the blood, 20 units of insulin was in 7 cases given before breakfast and the blood-sugar estimated at 15 minute intervals for 2 hours. The immediate effect was in most cases to produce a depression in the sugar curve. However, there are different degrees of sensitiveness to insulin in diabetics. Some patients become so easily hypoglycemic as to be thought hypersensitive to insulin. Most cases do well on 10 to 40 units a day; some require much bigger doses. Although the insulin dose often has to be diminished after a time, it is doubtful how far this is due to real improvement in the sugar tolerance or whether it is caused by an accumulation or late effect of the insulin. Jensen says that in no case of diabetes mellitus was it possible to demonstrate any definite improvement of the tolerance due to insulin. The insulin treatment was only found to be symptomatic for the defective sugar tolerance which is one of the manifestations of the metabolic disorder called diabetes mellitus. These rather discouraging conclusions may, perhaps to some extent, be explained by the fact that these diabetics were chronic cases where material alterations were hardly to be expected.

Since the introduction of insulin hypoglycemia is much more frequently met with than previously. How far hypoglycemia occurs in normal persons is not known to Jensen. Diabetics may become hypoglycemic on starvation, on certain diets, and practically always on the administration of insulin. It is the insulin hypoglycemia which gives rise to symptoms. How far hypoglycemia due to other causes than insulin may give rise to similar symptoms is doubtful. There is a recognized mode of death in diabetes, called the diabetic collapse, which is supposed to be due to heart failure, and which to a certain extent resembles severe insulin hypoglycemia.

Various symptoms have been described as due to overdosing with insulin or as features of hypoglycemia. Jensen has noted three kinds of symptoms often difficult or impossible to distinguish from each other.

The very mildest symptom of hypoglycemia is a feeling of hunger. Jensen does not treat these cases except to add a few ounces of vegetables to the diet. If the hypoglycemia becomes more severe, it is often the mental symptoms that are predominating. There may be in some cases profuse sweating all over the body. The first stage may gradually pass into a second, where the patient becomes increasingly more drowsy. Later he cannot be roused and sinks into absolute stupor. Another definite group is the motor symptoms. In the first stage there is often a certain amount of trembling, fear and mental alienation. In the more severe hypoglycemia this gives way to a motor weakness; there is loss of control. At the height of an attack the patient presents a striking picture and if this state is allowed to go still further he will pass into stupor without any symptoms of motor disturbance. Motor symptoms may occur as the patient comes out of stupor. They then take the form of tonic contractions. On the whole the symptoms of severe hypoglycemia often show a tendency to severe asymmetry. Respiration which, in most cases, is shallow and rapid, may occasionally be deep and heaving.

Treatment is well known and simple and clinical improvement always takes place fairly rapidly after the administration of sugar. In the rare and more severe cases Jensen used adrenalin to increase the blood-sugar.

It is now recognized that, besides the beneficial effect insulin has on the various pathological features of diabetes, it may in itself give rise to a number of symptoms.

Some of these may be considered results of over-action on the recognized diabetic symptoms, as the changing of hyperglycemia into hypoglycemia, acidosis into alkalosis, etc., thus producing the symptoms associated with these conditions. Others can be described as direct toxic effects, either of the insulin itself or of the substances injected along with it.

Jensen observed acute local reactions in one or two cases. They were simply inflammatory swellings and required no treatment. Chronic reactions are small cutaneous or subcutaneous circumscribed, painless areas of fibrosis. They are especially noticed on the arms of patients who have been having insulin for some time. Often they make it difficult to continue the injections in the area affected. If the area is rested and the injections performed elsewhere in the body the condition clears up after a few weeks.

Of all the complications met with in insulin treatment, the pains are the worst. The

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patient may get them from a few days to several months after he has started insulin. Two of Jensen's patients were doing fairly well on insulin treatment until the pains began. From this time their condition deteriorated. The pains may start in any part of the body, either in the site of the insulin injection immediately after it has taken place, or corresponding to a particular nerve, or some other part of the body, and they may spread to other parts of the body. In these generalized cases it has been the hands and feet that have been worst affected. The pain may last from one-half to a couple of hours or still longer, in some cases being constantly present. These latter cases deteriorate very quickly and it often becomes difficult to continue the insulin. In two cases Jensen was obliged to discontinue it. The milder forms yield to aspirin and other analgesics. Moderately severe cases do well on massage and electricity but severe cases remain refractory to all known treatment.

Effects of Partial Parathyroidectomy. — Frederick L. Gates and J. H. B. Grant. (*J. Exp. Med.*, **45** : 115, Jan. 1, 1927.)

Observations on the endocrine tissues of rabbits irradiated with a quartz mercury arc lamp have disclosed the striking hypertrophy of the parathyroid glands produced by the irradiation. Histologically, this hypertrophy was found to be a true hyperplasia of the endocrine tissue, but a study of the calcium and inorganic phosphate content of the blood of these rabbits failed to reveal any significant



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changes from the normal levels. The irradiation and consequent hypertrophy of the parathyroid glands, resulted in some degree of protection to the animals when part of the parathyroid tissue was extirpated. This fact indicates that the remaining hyperplastic tissue was potentially active, and that the increased factor of safety represented by this condition of the remaining tissue resulted in less loss of blood calcium, a more rapid initiation of recovery, and an absence of the rise in the inorganic phosphorus of the blood serum which was a characteristic result of partial parathyroidectomy in normal rabbits. A fall in calcium in all the irradiated rabbits, without a corresponding rise in phosphorus, shows that the drop in calcium is the primary reaction, and a rise in phosphorus a secondary reaction following parathyroidectomy. The relation of the rise in phosphorus to the development of tetany still remains obscure.

Course and Prognosis of Diabetes Mellitus in Children. — Gladys L. Boyd. (*Can. Med. Assn. J.*, **17** : 1167, Oct., 1927.)

The average length of life of the diabetic child has been lengthened by the use of insulin. Normal growth and development occur in the treated diabetic child. Diabetes in children is a rapidly progressive disease, which may not only be arrested in its course, but made less severe under adequate treatment with diet and insulin. The criterion of successful treatment consists in the absence of glycosuria and the maintenance of normal blood sugar for the greater part of the time. Fluctuations in tolerance are frequent, and gains may only be retained by fidelity to treatment. Pathological examination furnishes a certain degree of evidence, favorable to the belief that pancreatic regeneration may occur. The incidence of diabetic coma has not declined, but a material decrease in its mortality due first to insulin, and secondly to earlier recognition and treatment has occurred.

Effects of Injections of Calcium Chloride or of Disodium Hydrogen Phosphate. — Frederick L. Gates and J. H. B. Grant. (*J. Exp. Med.*, **45** : 125, Jan. 1, 1927.)

No significant differences were found in the reactions of irradiated, normal, or partially parathyroidectomized rabbits to injections of calcium chloride or disodium hydrogen phosphate. Intravenous injections of calcium chloride caused only a transient rise in blood calcium, which returned to its former l... within a few hours. The upper level of bl... calcium concentration is independent ... parathyroid control. Subcutaneous in... tions of disodium hydrogen phosphate cau... in all three groups of rabbits, a similar dep... sion of the blood calcium level. After la... doses of the phosphate solution, all of ... rabbits showed signs of acute tetany in wh... many of them died. Death or survival ... not determined, apparently, by the absol... depression of blood calcium. The rabb... that died were those, in all three groups, ... which a phosphorus retention carried ... initial rise in serum phosphorus to ev... higher levels in the hours preceding dea... and so changed the normal calcium-ph... phorus ratio to a small fraction of its for... value.

Effects of Inanition. — Frederick ... Gates and J. H. B. Grant. (*J. Exp. Me...* **45** : 139, Jan. 1, 1927.)

In these experiments the authors obser... the effects of complete inanition in irradiat... normal, and partially parathyroidectomi... rabbits to determine possible differences ... the fasting metabolism of calcium and in... ganic phosphorus with which the parath... roid glands, directly or indirectly, are ... essentially concerned. No distinctions co... be drawn between normal irradiated, a... partially parathyroidectomized rabbits ... the basis of their calcium and phosphor... metabolism. Blood calcium was reduced ... a similar manner in all three groups of rab... bits, and wide individual variations in serum ... phosphorus levels preclude significant dedu... tions. However, the irradiated rabbits s... fered disproportionate losses of weight dur... the fasting period and 4 or 5 of them died d... ing the course of the experiment. The dea... of these rabbits are attributed to this m... rapid consumption of their own tissues a... possibly also to suprarenal injury caus... both by fasting and by exposure to ult... violet light.

The Menopause. — Raymond G. C... (*Eclec. Med. J.*, **87** : 507, Nov., 1927.)

The climacteric is manifested by menstr... irregularities, dysovarism being its cen... disorder. The chief symptoms — men... physical, circulatory and metabolic — invo... practically all the endocrine organs, and ... proportion as they are related to the ovar...

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Enlargement of the thyroid is possible as a result of climacteric changes but rare. Hypothyroidism is much more usual. Eighty-five per cent of all cases of myxedema occur in women between the ages of 40 and 50. Obesity and metabolic insufficiency occur both in hypothyroidism and the menopause, also constipation. The most uniform of the results of hypothyroidism is cellular infiltration, with its train of symptoms. The estimation of the basal metabolic rate is an accurate measure of the extent of this fundamental change. An almost magical change in which chemical changes are reëstablished follows thyroid therapy. With the unloading of the puffy cells comes a reduction in size and weight of these patients. Marañon believes in an essentially climacteric type of rheumatism as a result of this slowed chemistry. He also states that there is an ovarian type of rheumatism not necessarily at the menopause, and explains that the ovaries require certain stimuli from the thyroid, while the thyroid, having many other tasks, may become functionally played out following acute infections, and consequently its detoxicating function may be defective. Resulting from this infiltration is menorrhagia. Another manifestation of the menopause, which is rare and necessarily a post-climacteric development, is the establishment of the masculine traits. This condition is known as virilism and is probably due to an undue compensatory function of the adrenal cortex.

Treatment is directed along three lines: (1) to lessen the suddenness and extremity of imbalance; (2) to give the organ a longer time and better chance of adapting itself; (3) to endeavor to remove the stress upon the overstrained organs. The last of these is a hygienic recommendation embodying rest, elimination, neutralization, and as suitable an environment as possible. In the second case ovarian therapy is the ideal treatment. In the first case, manifestations of hypothyroidism should be treated with some form of thyroid therapy. Corpus luteum is also given in these conditions. Pluriglandular therapy is often used with great success.

Ovarian Traumatization and Spontaneous Activity.—Ging H. Wang and Alan F. Guttmacher. (*Am. J. Physiol.*, **82** : 335, Oct., 1927.)

It has been shown that it is the secretion from follicular cysts which is responsible for the changes in both the activity of the organism and the structure of the accessory sexual organs found in rats whose ovaries have been moderately traumatized. The only cellular element constantly present in the follicular cysts has been found to be the granulosa layer. Thus, the granulosa cells may have given out the hormone which produced increased activity, cornification in the vaginal epithelium, and hypertrophy of the uterine wall.

Goiter. International Conference. — Berne. F. de Quervain. (*Lancet*, **213** : 1239, Dec. 10, 1927.)

Of special interest for the estimation of thyroid enlargement were the series of preparations set up by the pathological institutes of Freiburg (Aschoff) and Würzburg (B. Schmidt) dealing with the development of the thyroid at various periods of life, and in goitrous and non-goitrous regions. The life-curve of the thyroid, especially brought out by Aschoff, will contribute materially to a clear limitation between normal and morbid processes. If a survey is taken of material derived from various parts of Europe the conviction is soon reached that endemic goiter is fundamentally the same everywhere, and that local differences, apart from the absolute frequency of goiter, are due to relative frequency of the separate forms. In the center of a region where goiter is endemic, the nodular parenchymatous form prevails; at the periphery colloid goiter, diffuse at first, becoming nodular in later life; in the goitrous parts of the lowland separated from the great endemic centers diffuse colloid goiter only exceptionally becoming nodular.

Wegelin discussed the cretin goiter — the most severe form of goitrous thyroid change. The cretin's thyroid is either atrophic with little adenomatous nodules, or there lie in an atrophic matrix nodules of some size, as a rule of a parenchymatous character, in which all forms of secondary changes may occur — calcification, cyst formation, etc. In the cretin colloid is only occasionally formed in a goiter.

Williamson and Pearse drew a sharp distinction between secretion tissue and colloid storage tissue. Should the results of these two investigators be confirmed they would mark the greatest advance of recent years in our knowledge of this subject.

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De Quervain showed that the iodin level in the blood possesses great constancy, and that its height depends on the functional activity of the thyroid gland. It is at its highest in Basedow, at its lowest — only about half or so of the normal height — in the cretin. If the latter is given iodin in excess it is rapidly excreted, since his thyroid gland is not in a position to synthesize it in the normal way. On the other hand, the iodin in the thyroid is partly brought into another chemical combination, whether it is stored up as colloid or whether in this new combination it leaves the thyroid at once without being stored.

Crotti (Columbus, Ohio) found in the blood of goiter-bearers spirilla and protozoa of various kinds, a whole flora or fauna which he thinks he can show also in the water of goitrous neighborhoods. Folley (Paris) related similar independent findings and demonstrated them.

Sexual Indulgence and Growth. — James Rollin Slonaker. (*Am. J. Physiol.*, **82** : 318, Oct., 1927.)

Experiments were carried out with rats as to the effects on growth of varying amounts of sexual indulgence. Females showed greater differences in weight than the males. All groups of females showed a tendency to increase weight after the menopause. Sexual indulgence was associated with an increase in weight in the females and a decrease in amount of follicular hormone. Rats having sexual indulgence showed a tendency to grow more rapidly during early life than abstainers. The bearing of young at an early age appears to have inhibited body growth in later life.

Epinephrin in Progressive Myopia. — Meyer Wiener. (*J. Am. Med. Assn.*, **89** : 594, Aug. 20, 1927.)

The author believes that the stooping posture assumed by myopics for near work causes pressure on the suprarenal glands and has its influence on the progressiveness of the myopia. Properly conducted fresh air exercise brings about an added epinephrin output. Wiener says it seems fair to assume that both exercise and diet influence the secretion of the suprarenals, and that the local application of suprarenal secretion increases tissue metabolism.

Keith thinks that at the root of myopia there must be some fault in the mechanism which normally regulates the growth of the sclera. He asks, "Why cannot it be dysfunction of the suprarenals, or possibly the suprarenals in conjunction with some other gland

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Jean-Henri Dunant

(*Continued from page 17*)

culminated in a meeting in Geneva, in October 26-29, to which seventeen countries sent representatives and the legal background for the society was drawn up and an insignia chosen: a white band, later embellished by a red cross, virtually the coat of arms of Switzerland reversed. It was worn for the first time in the conflict between Denmark and Germany in 1864, by Dr. Appia, an official of the committee.

Things went well for several years until the failure of Dunant's business in Algiers and Tunis, which necessitated his withdrawal from the Society for voluntary aid. His creditors insidiously criticized him as a "hack writer who was not attending to his business." These assaults against his efforts made Dunant much depressed, so that he withdrew from himself. However, he again attempted welfare work to alleviate the distress of prisoners of war in Paris, but the disturbances in the Commune forced him to give up his efforts. Utterly heartbroken and poverty stricken, he disappeared into England, France and Germany for a long time.

In 1892 Dunant was discovered by a Swiss writer, Baumberger, working in a hospital in Heiden for three francs a day which kept him very modestly. Baumberger told his story in "Ueber Land und Meer" and Dunant again came before the public. The Empress Marie Feodorowna presented him with a pension and when the Nobel Peace Prize was first awarded in 1901, after much discussion and dispute, Dunant received the prize, amounting to about 208,000 francs, jointly with Frédéric Passy.

This sudden turn of fortune did not spoil Dunant, however, for he went on living in the hospital that had afforded him such pleasant refuge and there he continued his writings in the form of memoirs and articles for the cause of peace. It was his one wish that he be able to personally preside at the Monaco Congress for Peace, and to accept personally his peace award at Stockholm, but, unfortunately, his strength failed and death intercepted his plans on October 30, 1910.

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Parathyroid Preservation. — Wallace I. Terry and H. H. Searls. (*J. Am. Med. Assn.*, 89 : 966, Sept. 17, 1927.)

Millzner, by examination both of specimens removed at operation and of a series of cadavers, found a parathyroid on the anterior capsule of the thyroid gland in 10% and on the lateral capsule in 30% of cases.

Parathyroid Hormone and the Calcification of Fracture Callus. — Edwin P. Lehman and Warren H. Cole. (*J. Am. Med. Assn.*, 89 : 587, Aug. 20, 1927.)

The assumption that, because the injection of parathyroid extract increases the calcium in the blood stream, there will be more available calcium for deposit in fracture callus, is, in the opinion of the authors, a misapprehension that parathyroid extract is of such value. *A priori*, parathyroid extract should not offer aid in hastening or inducing the deposit of calcium in the soft callus about fractures. Its action is to mobilize the fixed calcium in the body. Hunter and Aub, who found that calcium excretion in patients is rapidly increased parallel to an increase in the blood serum calcium on the administration of parathyroid extract say, "The excess of calcium must have come very largely from the bones." The tendency is therefore toward reduction of the calcium in the bones.

The authors undertook a simple series of experiments which tend to support concretely the *a priori* reasoning above outlined. These experiments present evidence showing that favorable results in delayed union that have occurred following the use of parathyroid extract have not resulted from any beneficial action of the hormone. Indeed, if the injection of parathyroid extract has any influence on the rate of calcification of fracture callus, it is that of delaying the process.

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Cardiac Disturbances in Goiter.— John Phillips and J. P. Anderson. (*J. Am. Med. Assn.*, **89** : 1380, Oct. 22, 1927.)

In the study of a large series of cases of diseases of the thyroid gland the frequency with which disturbances of the heart are encountered, particularly in cases of hyperthyroidism is noticeable. These cardiac disturbances vary from a simple tachycardia, or tachycardia associated with various forms of arrhythmia, to cardiac decompensation with engorged liver, ascites and edema of the feet. The occurrence of auricular fibrillation does not appear to bear any relation to the type of goiter that may be present, but rather it appears to depend entirely on the presence and duration of the hyperthyroidism. It is most frequently associated, however, with colloid goiters with adenomatous nodules. Auricular fibrillation is most frequently associated with hyperthyroidism in persons over 45 years of age in whom some degree of arteriosclerosis is already present. Adenomas of the thyroid gland appear to produce cardiac irregularity in some cases before hyperthyroidism has been manifested by an increase in the metabolic rate. In every case of goiter, whether or not hyperthyroidism has been manifested, an examination of the heart should be made to determine the presence of any cardiac irregularity, as it is of the utmost importance that treatment should be instituted before serious heart injury has taken place.

One hundred and twenty cases of auricular fibrillation associated with hyperthyroidism are analyzed. In 75 of the cases in which operation was performed end-results could be obtained, and in 43 of these cases the action of the heart became regular after the removal of one or both lobes of the thyroid gland. The authors feel justified in concluding, therefore, that thyroidectomy is indicated in these cases. If the heart action does not become regular after thyroidectomy, treatment with quinidine may restore the normal rhythm. Even in cases in which the heart action is not restored to a normal rhythm, thyroidectomy will improve the heart action and the rate can be controlled by digitalis. The use of digitalis and of compound solution of iodin for from a week to 10 days prior to operation is advisable.

The Sulfur of Insulin.— Vincent ... Vigneaud. (*J. Biol. Chem.*, **75** : 393, ... 1927.)

Since evidence has accumulated that ins... is actually a sulfur-containing compound ... becomes imperative to discover the type ... sulfur linkage. If the active principle in ... actually contains sulfur, as is believed, ... the evidence presented in this study indic... that this sulfur is present as the disul... linkage and that insulin is most likely a deri... tive of cystine. Vigneaud found by means ... the phosphotungstic reaction that as ... insulin became more purified the cystine c... tent increased. The proportionality was ... striking that it gave hope that this m... prove to be a suitable means of assay ... purified preparations. When the sulfur ... split out, the disulfide linkage was destro... and the test for cystine greatly reduced ... intensity, indicating this as the source of ... labile sulfur.

Since it has been shown that insulin it... does not give the specific reaction (Sulliv... for cystine, and since the presence of cys... was demonstrated in the hydrolyzed ins... preparations, it must be concluded that ... cystine is present as some derivative. F... ther, the sulfur of the hydrolysate is co... paratively stable like free cystine, whe... the sulfur of the original unhydrolyzed ins... is very labile. This change of lability u... hydrolysis is identical with what would ... expected of an amino acid derivative of c... tine. Glutathione, for example, has a sul... lability of the order of insulin. Upon a... hydrolysis free cystine would be formed a... the sulfur of the hydrolysate would there... be stable.

The behavior of the sulfur in insulin is q... parallel to the behavior of the sulfur in am... acid derivatives of cystine and suggests t... the cystine in insulin is linked to the rest ... the molecule by a peptide linkage. In ... connection the high arginine, histidine, ... tyrosine contents of purified preparati... might be recalled.

In Abel's analyses the calculated empir... formula of $C_{45}H_{75}O_{17}N_{11}S$ is based upon ... presence of 1 sulfur atom in the molec... From the author's work on the presence of ... disulfide linkage the minimum value w... have to be twice that given, or $C_{90}H_{150}O_{34}N_{...}S_2$.

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Hyperthyroidism and the Autonomic System. — Lemoine. (*Presse méd.*, **37** : 440, Apr. 3, 1929.)

M. Lemoine affirms that it is very difficult for clinicians to theorize and explore the vegetative system. He subjected hyperthyroid patients to Danielopolu's atropin test which seems to him to be the best method of sympathetic investigation. Exophthalmic goiter patients were shown to be sympathicotonic according to this test. In order to corroborate this result, M. Lemoine practiced a bilateral cervical sympathicotomy in a hyperthyroid patient. The patient's condition was transformed: fall of metabolism, slowing of the pulse, present tendency to obesity.

Remote and Immediate Results of Treatment of Hyperthyroidism by Short Radiations. — M. Sluys. (*Presse méd.*, **37** : 440, Apr. 3, 1929.)

It seems that the healthy thyroid gland is refractory to the rays. The proof is found in the slight variations of somatic morphology and histology of the gland and respiratory exchanges after very intense expositions of the cervical region for metastases or adenitis. If the rays have an action it is indirect: influence on lymphoid circulation. Very atypical cases and very severe cases should be subject to the rays. Applied with care they no longer give surgical complications. When it is a question of ovarian hyperthyroidism, the results are always good, but more unstable. In all cases medical collaboration is indispensable.

New Classification of Hyperthyroid States; Iodin Treatment of Hyperthyroidism. — Dautrebande. (*Presse méd.*, **37** : 440, Apr. 3, 1929.)

Goiters may be divided into: goiters with normal metabolism (simple goiters of adolescence or colloid goiter, simple adenomatous goiter with degeneration) and into thyroid hypertrophy with increase of metabolism. This latter group includes exophthalmic goiter, severe toxic adenoma, benign toxic adenoma, finally clinically atypical hyperthyroidism. This latter may have two aspects: either that of a simple goiter with raised metabolism, or not presenting any morphologic modification of the thyroid but bearing the characteristics of a nervous tachycardia with raised metabolism. In these two cases, thyroidectomy or ingestion of Lugol's solution is effective. A good sign of hyperthyroidism is the increase of differential arterial tension (Read and Davies).

Dautrebande's first works on the effects of iodin treatment have received their confirmation by numerous foreign authors. In medical therapeusis, iodin will act, provided it is administered continuously, in large doses and in fractioned manner.

Insulin in the Treatment of Hyperthyroidism. — Goffin and J. Slosse. (*Presse méd.*, **37** : 440, Apr. 3, 1929.)

The authors administered as much as 6 clinical units to patients in whom the usual treatment had been ineffective. They were able to follow results for two years. In the majority of the cases studied, the authors noted slowing of the pulse, increase in weight and decrease of basal metabolism.

The Most Important Hormonal Disturbances of Childhood and Their Treatment. — R. Wagner. (*Wien. klin. Wochenschr.*, **41** : 1689, 1928.)

In the hormonal therapy it is important to determine whether the internal secretion prepared from the gland can replace the function of the gland concerned when introduced into the body. Up to the present, three such internal secretions are available: thyroxin, parathormone and insulin. Adrenalin and pituitary have, to be sure, a marked pharmacologico-dynamic activity, but are not to be considered as bearers of a substitution therapy. Thyroid treatment is of greatest importance practically. Thyroxin as well as the oral administration of desiccated thyroid comes into consideration here as complete substitution therapy. Pituitrin is an excellent symptomaticum for definite forms of diabetes insipidus, but must be injected 1 to 2 times daily, continuously, like insulin.

Contribution to the Organotherapy of Obesity. — H. Ueberall. (*Med. Klin.*, 1839, 1929.)

Although thyroid preparations are to be named as remedy of choice in endogenous obesity, there are forms of obesity which, although conditioned endogenously, do not respond to thyroid medication or make it impossible through pathological reaction.

The circumstance that pure, monoglandular forms of obesity probably do not occur and

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attempt at polyvalent treatment, led to the preparation of pluriglandular reducing agents. These preparations are to be preferred to pure thyroid medication; still they contain thyroid in addition to other substances. For cases which are sensitive to thyroid medication there are also thyroid-free pluriglandular preparations.

The therapy is tolerated without untoward symptoms. Increases in basal metabolism and decrease in weight give evidence of the activity of the medication, even when used for a long period of time without reduction of diet, which is itself by no means inferior to thyroid medication.

Prognosis and Therapy of Intermittent Claudication and of Incipient Gangrene of the Extremities. — H. Schlesinger. (*Med. Klin.*, **25** : 18, 1929.)

The idea certainly is strongly suggested of causing a marked vaso-dilatation through organotherapeutic measures. The author repeatedly used a preparation prepared from normal vessel walls (albumin-free), which was given intravenously 1 to 2 injections a week in doses of 5 to 10 cc. According to the experiences up to the present the measure seems to exert a favorable action on the disease process, but is apparently not superior to the nitrites.

Owing to the preponderance of the disease in the male sex, it can be assumed that the female sex glands exert a protective influence on the vessel wall; proceeding from these considerations the author repeatedly attempted the treatment of this disease with ovarian preparations, in men. Concerning the results of this method of treatment, which are not yet settled, the author will make a report later.

Concerning the Point of Attack of Insulin. — Bürger and Kramer. (*Münch. med. Wochenschr.*, **76** : 178, 1929.)

Experiments of the author show with certainty the fact that the action of insulin on carbohydrate metabolism is united to the co-operation of the musculature. In the first 20 to 40 minutes after the intravenous injection of insulin there regularly occurs in man and in dogs an increase in blood sugar (primary paradoxical insulin hyperglycemia) which remains absent when the liver is removed from the circulation and on the other hand becomes maximum following the injection of 2 units per kilogram dog into the trunk portal vein.

Concerning Capillary Microscopy in Children. — Doxiades. (*Verein inn. Med. u. Kinderheilk., Berlin*; Session of Jan. 28, 1929.)

In fainting fits the visible capillaries become empty. Adrenalin increases the amount of circulating blood. If thyroxin is administered for a long time, the capillary picture frequently becomes normal.

The Early Diagnosis of Pregnancy from the Urine Through Administration of the Pituitary Anterior Lobe Hormone (Zondek-Aschheim Reaction). — Ehrhardt. (*Münch. med. Wochenschr.*, **76** : 82, 1929.)

The author tested the Zondek-Aschheim reaction in 197 cases and obtained correct results in 194 cases. In the preponderant majority of cases the diagnosis could be determined macroscopically.

Concerning Treatment of Female Sterility. — K. Amersbach. (*Münch. med. Wochenschr.*, **76** : 15, 1929.)

The author reports concerning a case in which the serologic test showed marked hypofunction of the pituitary and ovary. Accordingly, a corresponding etiologic therapy was given: namely, organotherapy with anterior pituitary preparation combined with ovarian preparations, at the same time diathermy and light stimulative radiation of the ovaries. The result of this treatment was at first regulation of the menses, later actual pregnancy. In another case in which sterility appeared in amenorrhea due to hypofunction of the ovaries, in hypofunction of the thyroid and later adiposity and growth of hair on the cheeks, thyroxin, an ovarian preparation, diathermy and balneotherapy were prescribed. Result: loss of 14 pounds in weight, appearance of slight menstruation once. Up to the present time no pregnancy; growth of hair on the cheeks uninfluenced.

Treatment of Diabetes with Pneumothorax and Insulin. — L. M. Blum. (*Paris méd.*, **19** : X, 92, 1929.)

In addition to cases in which insulin treatment undoubtedly has a favorable action, some also come under observation in which insulin effects a more rapid development of

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pulmonary processes. Nevertheless insulin therapy is always to be tried and when possible to be combined with application of a pneumothorax.

Concerning Insulin-Forced Alimentation. — Fellegi. (*Med. Klin.*, **25** : 263, 1929.)

Since opinions concerning insulin-forced alimentation are still divided, the viewpoints coming into consideration should be discussed. (1) The foundation of a successful treatment is the administration of proper doses. Small doses of insulin give results only when it is a question of quite healthy persons, who despite good appetite are unable to take on weight. (2) Insulin is to be given in increasing dosage. (3) The result of treatment depends on the course of the hypoglycemic reaction. The prescription of the exact time of food intake is not correct, since the appearance of the hypoglycemic reaction depends not only on the size of the dose but also on the sensitiveness of the patient to insulin. (4) The meals should not begin with the eating of carbohydrate. (5) Immediately before injection nothing should be eaten. (6) Glucose should not be injected at the same time as the insulin. (7) Insulin is indicated only when the gastrointestinal tract is free from organic changes. (8) The increase in weight obtained during the insulin treatment continues even after termination of the treatment. (9) In patients with pronounced dyspeptic complaints, good results are obtained when a pancreas preparation is prescribed at the same time as the insulin. (10) According to the author's experiences insulin is not contraindicated in chronic, fibrous and fibrocavernous forms which show merely moderate rise in temperature and mostly a slow course. In the insulin treatment of tuberculosis, the prevention of a possible hypoglycemic reaction is especially important.

The Action of Pepsin on Insulin and Its Acetyl Derivative. IV. Contribution concerning Insulin.—W. Dirscherl. (*Hoppe-Seylers Zeitschr. physiol. Chem.*, **180** : 217, 1929.)

In extensive measurements Dirscherl found that the action of pepsin on insulin is irreversible and may not be made to retrograde. The author agrees in this with the findings of A. Harteneck and W. Schuler.

Further experiments show that the action of pepsin on insulin fits into the category of a ferment action; in particular the dependence on time and temperature does not fit the opinion that the inactivation of insulin can be occasioned by an absorption of pepsin. It can be admitted especially that the inactivation of insulin through pepsin rests on a decomposition of albumin. If insulin itself is an albumin substance, it must belong to that complicated type which is affected by pepsin. In the treatment of suspended acetyl insulin with pepsin, the influence is very limited.

Formaldehyde inactivates insulin in pH 7 in a moderate time reaction. The preparation may be precipitated and is again brought to an activity of about 25 per cent of the original insulin by heating with N/10 hydrochloric acid. In this treatment with acid and heat the active portion is precipitated. Insulin itself behaves quite similarly in the presence of hydrochloric acid in heat. Blatherwick and his associates also found insoluble insulin fractions.

Anemia in Rats and Liver Treatment — A. Orban. (*Monatschr. Kinderhlk.*, 4 402, 1929.)

The following conclusions are to be drawn from the rat experiments undertaken. (1) Liver feeding does not have an accelerating action on the blood regeneration in rats which have been rendered anemic through withdrawal of blood, even when liver extract or liver residue is given. (2) Feeding of liver is unable to accomplish a vitamin effect under the experimental conditions prepared by Orban. (3) Since an accelerating action on blood regeneration did not appear in the experiments mentioned, the action of liver does not appear to be a simple stimulus to regeneration.

Concerning the Influence of Atropin, Adrenalin and Amyl Nitrite on the Size of the Heart. — D. Scherf and E. Zdansky. (*Wien. klin. Wochenschr.*, **42** : 60, 1929.)

Following intravenous injection of 0.5 cc. of 1 per cent solution of adrenalin an enlargement of the heart was never observed in individuals with normal heart and blood vessels, but in a part of the cases a distinct diminution could be deduced from the kymographic curves. An enlargement was only observed when the blood pressure rose or

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200 mm. mercury. This is explained by the fact that the heart reducing, positive inotropic action and the acceleration of frequency were equal to or even surpassed the heart enlarging action of the rise in blood pressure. In several cases in addition to the diminution of cardiac caliber, a diminution of the size of excursion of the cardiac rims was present which may be in all probability concluded to be a decrease of cardiac output.

Modern Treatment of Skin, Urinary and Sex Diseases.— H. Colman. (*Med. Klin.*, **25** : 192, 1929.)

In acne vulgaris in addition to other preparations and purgatives an organotherapeutic treatment with preparations such as lutein, thyronucleoprotein, adrenucleoprotein is to be used as internal medication.

Therapy of Paroxysmal Tachycardia and of Extrasystole. — E. Maliwa. (*Mitt. Volksgesdhtsamtes*, **1** : 23, 1929.)

In many cases it is sufficient to use quinine and quinidin. There are, however, cases refractory to quinine. In such cases it is recommended that 1 cc. adrenalin in 10 cc. physiological salt solution be injected intravenously.

Treatment of Adiposity. — H. Erdman. (*Die med. Welt*, **3** : 169, 1929.)

Among the therapeutic measures endocrine preparations are also to be mentioned, especially the thyroid hormone which furthers metabolism. Thyroid preparations can also be of assistance in obesity due to over-eating, but they have a great disadvantage: they have a harmful effect on the heart.

The Thyroid Problem. — Walter M. Boothby. (*Endokrinologie*, **3** : 1, 1929.)

Thyroxin is a catalyzer which accelerates the production of heat by increasing the basal metabolism. It is of importance practically that the curve of the fall of the thyroxin action takes its course according to definite mathematical rules. The action of thyroxin on growth and physical and psychic characters is to be considered as secondary. The treatment of myxedema is to be directed towards two goals: (1) elevation of the production of heat through increase of thyroxin concentration in the tissues to the normal value and maintenance at the normal value. Accordingly the dosage should be sufficiently large in the first week, that a decided surplus is present. The treatment should be a lasting one and not intermittent and the amount of thyroxin given daily following the initial period should be exactly the amount of that destroyed daily. The amount of thyroid preparation required is of course dependent on its thyroxin content; since the normal amount of thyroxin in the body is somewhat less than 14 mg. This amount must accordingly be given. With regard to endemic cretinism it must be said that possibly a limited number of cretin cases (hypodysthyrosis of de Quervain) may be treated successfully if iodin were combined with desiccated thyroid.

The Eye in General Medicine. — A. Patry. (*Rev. méd. Suisse Rom.*, **49** : 29, 1929.)

Hypertrophy of the endocrine glands calls forth eye disturbances of mechanical nature. To this group belong the manifestations of exophthalmic goiter, conjunctival congestion, recurring hemorrhages of the vitreous humor in juvenile hyperthyroidism, the retinal spasms through disturbances of equilibrium of the thyroid or ovary. Baillart found spasmodic crises in a case of dysmenorrhea. Administration of thyroidin changes the ocular pressure. Muller effected distinct improvement in three cases of glaucoma through pituitrin. Trophic disorders, blue sclera, brittleness of bone are to be attributed to polyglandular etiology and hypoglycemia or dysfunction of the parathyroids. We are familiar with forms of cataract due to genital, parathyroid and thyroid disturbances. Endocrine cataract belongs in the range of internal secretory disorders. It develops during pregnancy as well as at the time of involution of the sex glands. The cataract of old people is to be attributed to a profound disturbance of the endocrine glands. Sigrist was able to extract a hormonal substance from the parathyroids with which he treated cataract cases with some success. Diabetes promotes and at least accelerates the appearance of "senile cataract."

Therapeutic Attempt in Urticaria. Allergic Diet. — Teran Argüelles. (*Zentr. ges. Kinderheilk.*, **22** : 676, 1929.)

After various investigators had made the observation that spleen extract suppresses

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eosinophilia, pruritus, asthma and other allergic diseases or at least assuages them, the author attempted to treat severe cases of urticaria in children with spleen extract. The extract was administered before meals and influenced cases favorably which had remained refractory to every other therapy.

The Cholecystographic Test of Motility of the Gall Bladder and Its Results. — H. Bronner. (*Fortschr. Geb. Röntgenstr.*, **39** : 23, 1929.) (The Test of Evacuation by Means of Pituitrin Injection, page 29.)

The introduction of pituitary preparations used by Kalk and Schöndube as measure for the determination of the gall-bladder content, possesses extraordinary certainty of action according to several publications of these authors and also of other authors. Several exceptions to the action were also determined; the degree of evacuation of the gall bladder obtained was, however, subject to strong variations. If a whole series of authors have frequently observed only a partial evacuation, this circumstance doubtless serves to lessen the usefulness of the method for clinical cholecystography. It is important to stress in this connection that several authors could determine a decided cholekinetic superiority of physiological food stimulus as opposed to pituitary preparations in comparative investigations and Bergmann noted: among the cholekinetics, pituitrin is only one, and not the strongest. As the strongest agent to obtain the condensed cystic bile, the emulsion of egg yolk in oil may be considered. Bronner also believes that the pure yolk meal is to be recommended as the useful and reliable normal procedure for the clinic.

Hyperglycemia and Senile Cataract. — J. Galindo. (*Med. Ibera*, **24** : 482, Apr. 13, 1929.)

Recent studies of Marañón and other authors have shown the presence of symptoms and complications of diabetes in patients without glycosuria, but with spontaneous or induced hyperglycemia. The author systematically investigated the blood sugar curve in his cases of cataract and found that 58.5 per cent of the cases were either plainly diabetic or presented curves of prediabetic hyperglycemia. It was not possible to determine in these cases whether it was a question of actual diabetic cataract or of senile cataract coincident with the diabetes. Although the genesis of diabetes is very obscure it is evident that its production is related to metabolic disturbances, principally of diabetic type. In the author's opinion, an analogous pathogenesis should be invoked to explain glaucoma. From the practical viewpoint, the knowledge of these cases is normally important. The oculist is accustomed to analyze the urine and not to operate without a preliminary treatment of the diabetic patients. If there is sugar in the urine, however, he considers the to be healthy when it may be a question of latent hyperglycemia. Another interesting aspect of the question is the possibility of treating cataract medically. Joslin has already pointed out the interesting fact that the opacity of the lenses in incipient diabetic cataract decreases with the general treatment and with the improvement in the diabetes. It seems to be a certain fact that cataract is related to hyperglycemia by the frequency with which it is present in young diabetics who have suffered the disease for many years. On the other hand the significant fact of having found 58.5 per cent of cataracts in hyperglycemia coincides with the opinion of Marañón and the observation of two patients with incipient cataracts who have been subject to adequate diet since October, and who at the present time have their cataracts arrested and preserve the same vision, inclines the author to think of the possibility of a medical treatment of cataract. In order to do this, an early diagnosis of cataract is of great importance. For this purpose, the corneal microscope and the slit lamp are very useful. Once this early diagnosis has been made and in case this is positive and shows an alteration of carbohydrate metabolism medical treatment of the cataract should be undertaken with diet and small doses of insulin.

The author's opinion concerning the time for operation of diabetic cataract is that before operating the cataract an analysis of blood sugar should be made to determine the curve of glycemia. With respect to the condition in which a diabetic should be in order to be operated upon, he agrees with the work of Marañón and Blanco Soler that diabetic patients in order to be operated upon should be without glycosuria and with normal blood sugar, during the operation as well as post-operatively.

In the discussion, Dr. Nogueras stated that he had seen some cases of cataract which

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hyperglycemia but without glycosuria. In incipient cataracts he had observed improvement produced by insulin, including a case with normal blood sugar curve.

Investigation concerning the Influence of Various Altitudes on the Action of Thyroid in the Dog. Contribution III. — R. E. Mark. (*Naunyn-Schmiedebergs Arch. exp. Pathol. u. Pharmakol.*, **139** : 68, 1929.)

The action of various diets on hyperthyroidization at an altitude of 2000 m. was investigated. It was found that slight undernutrition of dogs with carbohydrate as well as meat diet is tolerated with less loss of weight at an altitude of 2000 m. than on the plane level. Definite nitrogen retention exists at this level. The water requirement was greater with the same diet at this level than in the later experiments on the plane level. In dogs which in preliminary experiments on the plane had shown complete hyperthyroidization, essentially weaker thyroid action appeared at the higher level. In animals again brought to the plane an after-effect of the higher level existed for about 3 weeks. Hyperthyroidization was of course far inferior to the action of the thyroid doses in the preliminary experiment.

Blood Sugar Investigations in Diabetics Treated with Insulin. — N. A. Nielsen. (*Zeitschr. klin. Med.*, **109** : 637, 1929.)

The blood sugar was tested every hour for 24 hours in 8 diabetics under insulin treatment. It was shown that the test of the morning blood sugar alone did not give a clear picture of the action of insulin on diabetic hyperglycemia, in any of the patients. The value, measured 5 hours after insulin in all these patients, lies at a more or less pronounced level of the curve, at its minimum or close to it. This is the case following the injection in the morning, after the injection at night and also when the dose is changed. This value accordingly gives a far better picture for the action of insulin on the blood sugar. Through determination of the blood sugar before and 5 hours after the injection of insulin we obtain a good idea of the appearance of the 24 hour curve, since this takes its course equally rising or falling between two values. If two injections are given, the best picture is obtained through determination before and 5 hours after each injection. From the curves it is shown that under insulin treatment, sugar analyses must be undertaken on portions of the urine, which are excreted shortly before the injection of insulin, since the blood sugar is highest here. Moreover, it is recommended that a portion of the urine which has been excreted several hours before the morning injection be examined in severe cases, since this portion will certainly be free from sugar, owing to the late and steep rise in blood sugar in some cases. The behavior of the curve corresponds to the clinical estimation of the severity of the case, since in more moderate forms of the disease curves with slighter oscillations are found and in more severe forms of the disease, curves with greater oscillations occur.

Concerning Bronchial Asthma. — M. Matthes. (*Wien. med. Wochenschr.*, **79** : 214, 1929.)

The acute attack of asthma must, to be sure, be controlled as actively as possible. Adrenalin is the most effective in the majority of cases. In general this therapy is harmless even though we do occasionally find individuals who respond to the injection with violent cardiac activity. That continued use of adrenalin leads to obesity as Lorand maintains, the author has never observed. Outside of adrenalin the author also uses ephedrin and synthetic ephedrin, antipyrin and caffein.

Revivification Experiment on Desiccated Animal and Human Organs. — Morosow. (*Die med. Welt*, **3** : 153, 1929.)

The author studied the action of various pharmacologic preparations on the blood vessels of the mummified rabbit ear. The drugs used were adrenalin, nicotin, cocain and caffein. Caffein exerted no action on the ear vessels, although it was introduced in high concentration. All the vaso-constrictor preparations exerted their characteristic action on the blood vessels, but in a slighter degree than normal. Thus, for example, the vessel lumen contracted not more than about 68 per cent upon the introduction of 1 cc. adrenalin in a solution of 1:1000, whereas a similar dose into the vessels of normal organs occasions complete and exceedingly long continued spasm. Isolated frog heart which has been desiccated to 25 per cent loss of weight and flushed with Ringer's solution showed contractions which, though weaker than normal, continued for many hours and were increased

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in their frequency and intensity by the addition of L. Haberlandt's hormone of heart motion. The author believes that the experiments which were also undertaken on hearts of human embryos, suggest a hitherto not accepted property of the tissues of vertebrates and outside of their general biological significance they also have a positive interest for the practicing physician.

Pituitary Dwarfism. — H. Lucke. (*Zeitschr. Konstitutionslehre*, **14** : 430, 1929.)

Report concerning a case in which, through successful organotherapy, evidence of pure pituitary disorder (diagnosed from the clinical picture) was obtained. It was even found that these diseases may be influenced to such an extent through substitution treatment of sufficient duration that these often psychically normal dwarfs can take up the struggle for existence like other normally grown individuals through the possibility of approximation of their physical form to the normal. In the author's case it was a question of a 12½ year old girl (4 years ago), who was born normal, but remained backward in physical growth for several years. On the basis of established findings a disease of the pituitary was assumed — an insufficiency of the anterior lobe. Recourse was had to organotherapy and treatment with pituitary anterior lobe introduced. The child first received one injection daily, later three, and then 2 tablets daily. The child is now 15 years old, still somewhat small, but certainly not to be described as a dwarf. She grew about 28 cm. within 1½ years. The anomalies of metabolism have also adjusted themselves extensively.

Unusually Large Thyroid Dosage. Its Dangers: Case Report. — L. E. Parkins. (*New England J. Med.*, **200** : 231, 1929.)

Report concerning a patient who in a period of time of 4 years took 667.3 gm., accordingly an average daily dose of 0.53 gm. thyroid extract. The patient had dyspnea, severe cyanosis, pulmonary edema and great amounts of blood tinged sputum. Thyroid medication was of course immediately discontinued and morphine and bromide given. After 10 days the patient had recovered and was dismissed able-bodied. The author draws the conclusion that thyroid extract treatment in obesity should not be undertaken without determination of the basal metabolism, that, moreover, a long continued use of the remedy in large doses can cause tachycardia, dyspnea and acute pulmonary edema, that the remedy does not act locally in the usual doses.

A Case of Cryptogenetic Pernicious Anemia Resistant to Simple or Mixed Liver Treatment. — P. Émile-Weil. (*Presse méd.*, **37** : 521, Apr. 20, 1929.)

The author reports a case of cryptogenetic pernicious anemia diagnosed clinically and corroborated by necropsic examination, which proved to be resistant to liver treatment, as well as to transfusions completed by insulin therapy. Then within 1 month he obtained an important improvement (gain of 9 pounds, rise of blood cell count from 1,000,000 to 2,700,000, fall of globular value from 2 to 1) by combining the various methods. The patient left the hospital for the country but returned at the end of 6 weeks with recurrence and the treatment which had been effective before the recurrence, no longer gave any result. Death occurred at the end of 2 months with the blood in a state of panmyelophthisis.

On the subject of this case the author speaks of cases of Biermer's disease which proved resistant to liver.

In the discussion, N. Fiessinger stated that he had also observed failures with Whipple's method in pernicious anemia. One case in particular in which the blood formula had returned to normal at the end of a month's treatment with liver, presented new signs of pernicious anemia 4 months after cessation of the treatment. This time the disease was not modified by liver nor by liver extracts. In two other cases in which it was a question of aplastic pernicious anemia, he was unable to obtain results with Whipple's method. It would seem that the Americans have especially treated cases of plastic pernicious anemia, it is in these forms that the reaction of the blood cell picture which they describe, observed.

M. Tixier reports failures of Whipple's method, in cases of pernicious anemia in childhood especially, which appear to be more difficult to treat than that in adults. It is possible that the extracts of liver act like insulin in diabetes, Biermer's disease continuing to exist.

P. Émile-Weil draws attention to the fact that in his case the anemia was not entirely aplastic. Liver extracts are useful but have not the same value as liver in nature.

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M. Monier-Vinard stated that even though he had obtained marvelous results with Whipple's method in pernicious anemia, he had noted its ineffectiveness in another form of severe anemia, the anemia of benzine poisoning where he observed no sign of restoration of the blood picture. In these cases there is a considerable diminution of polynuclears which persists despite liver treatment and perhaps the prognosis might turn to profit the comparison of the variations of the leucocyte formula.

P. Émile-Weil stated that he was also unable to influence benzolic anemia and anemia due to thorium by liver treatment. In several cases of severe anemia due to arsenobenzol he noted that the first improvement is a modification of the leucocyte formula. No characteristic permits one to separate these different anemias or to know whether the medicine will act.

M. Chevallier distinguishes two entirely different groups of affections. Pernicious anemia on the one hand and hemorrhagic aleukemia on the other, the latter being characterized by a marked anemia with considerable diminution of white cells and especially of polynuclears, hemorrhages and an absolute resistance to all types of therapy. The prognosis of the severe anemias is governed in his opinion by the modifications of the white cells.

Basic Properties of the General Regeneration Hormone. — R. Fraenkel. (*Arch. klin. Chir.*, **154** : 398, 1929.)

In experiments which were performed independently of the works of Lorin-Epstein, the author found that in warm blooded animals and also in human beings the course of regeneration is guided by furthering and inhibiting substances in the blood: a substance which kindles the growth of the regeneration but in general inhibits the differentiation and another substance which accelerates differentiation, hence inhibits growth. The plastic hormone can not be identical with the decomposition substance absorbed. Since its action increases exactly parallel with its amount, it may be assumed that the absorption of decomposition substance causes a formation or appearance of the plastic hormone. The possibility also exists that this arises secondarily from the decomposition substance. The site of formation or transformation is unknown.

Lorin-Epstein considers the differentiation hormone as an antibody against the decomposition substance. This conception can not be correct. A further difficulty rose with the knowledge that decomposition substance and plastic hormone are not identical; for in this way the direct relation of the differentiation hormone (first appearing later) with the decomposition substance becomes especially doubtful. It is conceivable that the differentiation hormone is directly transformed from the plastic hormone. In any case it is shown that to an increased formation of the plastic hormone there corresponds, later, an increased action of the differentiation hormone. The guiding substances acting on the regeneration processes (following injuries) from the blood correspond to the definition of functional nature which Asher has given for hormones. They should accordingly be correctly designated as plastic and as differentiation hormone.

The actions of both hormones depend on the "disposition" of the regenerating tissue.

Concerning the Effects of Liver Therapy in a Severe Post-Hemorrhagic Anemia in an Azotemic. — Labbé, Boulin, L. Justin and Gouven. (*Presse méd.*, **37** : 209, 1929.)

Report concerning the course of the illness and the results of treatment in a patient who suffered from chronic azotemic nephritis and showed symptoms of severe anemia following metrorrhagia caused by a fibroma. Under the influence of a liver treatment (administration of liver extract) the regeneration of the constituents of the blood set in very rapidly. The red blood cell count tripled within a period of 14 weeks, although the existing azotemia showed an essential increase.

Concerning the "Hormone" of Spontaneous Uterine Contractions. — J. Voegel and N. Margolina. (*Arch. Gynäkol.*, **135** : 478, 1929.)

The study of the spontaneous contractions of the smooth musculature is considered at the present time from the new "hormonal" standpoint. Le Heux cleared up the properties of cholin — of the "hormone" of the intestinal wall; it is secreted in the contractions of the intestinal wall and is able to induce movements of the intestinal musculature and to strengthen them. The "hor-

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mone" of heart motion has specific action according to the opinion of Demoor and Haberlandt and possesses specific properties of the known hormones. The authors obtained the following results with regard to the uterus in their experiments: an isolated uterus (rabbit's) cornu which had remained in Ringer-Lock's solution (R-L) with continuous current of air or O_2 administration, after normal, automatic, rhythmic contractions of 10 to 12 minutes, begins to give stronger and more frequent contractions which at times assume a tetanic character (asphyxia of the isolated piece). If the Ringer-Lock solution in which the isolated piece of uterus had been is replaced by pure Ringer-Lock solution, the tetanic character of the contractions disappears and the latter again become rhythmic.

The isolated piece of uterus gave the same regular rhythmic contractions in flowing Ringer-Lock solution for hours. The R-L solution in which an actively contracting rabbit uterus had been present for 2 to 3 hours, stimulates the contractions of this isolated organ. The Ringer-uterus solution possesses no individual specificity. Its chemical investigation reveals: (1) a decrease of alkalin reaction, (2) a decrease of the glucose content and (3) a rise of the calcium content in comparison with pure and flowing R-L solution in those cases where it had exerted a contraction-stimulating action.

Pancreatic Function. IV. The Humoroneural Regulation of the Gastric, Pancreatic and Biliary Secretions. — S. Okada, K. Kuramochi, T. Tsukahara and T. Ooinoue. (*Arch. Int. Med.*, **43** : 446, Apr., 1929.)

In general, epinephrin inhibits the secretion of digestive juices and insulin accelerates it. The mechanism of this inhibitory and excitatory action, however, is unknown. The purpose of this study was to solve the *modus operandi* of the regulatory mechanism of the secretion of the digestive juices, so necessary for the welfare of man and animals.

The authors found that:

1. Insulin provokes gastric, pancreatic and biliary secretion, and epinephrin inhibits it (only the influence of epinephrin on the gastric secretion is not so decisive). Ephedrin has an effect similar to that of epinephrin. The increased secretion of these juices after the injection of insulin is marked in the presence of a pronounced hypoglycemia, while it is nearly negative in the absence of hypo- cemia. The decrease of the secretion of ... juices after the injection of epinephrin ... parallel with hyperglycemia, and is follo... by an increase of secretion when a reac... hypoglycemia occurs.

2. Also in cases of cancer of the stom... in which the gastric juice remained alka... during the course of the collection, a mar... increase of the secretion of pancreatic a... biliary juices after the injection of ins... was observed, indicating that insulin ... marily stimulates the secretion of these ju...

3. The increased secretion of gastric a... pancreatic juices and of bile induced by ... injection of insulin is almost comple... inhibited by an injection of dextrose, bu... profuse secretion again occurs when hy... glycemia recurs. Therefore, it is defini... shown that hypoglycemia, if it does not al... stimulate the secretion of these juices, does ... when insulin is injected.

4. An injection of atropin causes a di... tinct inhibition of the increased secretion ... these juices induced by the injection ... insulin, indicating that hypoglycemia ex... its stimulating effect on the centrum of ... secretory nerve and that the stimulus ... transmitted to the acting tissue cells thro... the parasympathetic nervous system.

5. When dextrose is introduced into ... duodenum, it usually brings about an imm... increase of the secretion of pancreatic ju... and of bile, perhaps as a reflex evacuation ... the gall and pancreatic tracts, including t... gall bladder. Hyperglycemia, after resorp... tion of the dextrose, however, stops th... secretion of pancreatic and biliary ju... almost entirely, and the gastric cont... becomes achlorhydric. Following the hyp... glycemia, a reactive hypoglycemia is eve... which is accompanied by a profuse secreti... of digestive juices. An intravenous injecti... of dextrose has almost the same effect, exc... that the initial increase usually does ... occur and the diminution of the gastric se... tion is manifested in amount rather than ... acidity. An isotonic or rather a somew... hypotonic solution of dextrose has the s... inhibitory influence on the secretion of ... digestive juices as a hypertonic solution, if ... amount is sufficient. Therefore, it is d... nitely proved that hypoglycemia, in gener... stimulates the secretory nervous centr... and hyperglycemia inhibits it and that ...

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stimulus is transmitted through the parasympathetic nervous system to the reacting tissue cells, while the inhibitory impulse most likely is transmitted through the sympathetic nervous system.

6. The test breakfast does not cause any secretion of acid or cause a markedly diminished secretion of acid by the stomach at the stage of hyperglycemia, in comparison with its effect on the secretion of acid at a time of fasting. The motility of the stomach is also inhibited, so that the bread remnants of the test meal are detectable for a much longer time by fractional suction. Hypoglycemia is accompanied usually by hunger and hyperglycemia by a "full feeling."

7. Since hypoglycemia induces a humorally excitatory impulse and hyperglycemia an inhibitory impulse to the secretory centrum and since from this centrum the stimulus and the inhibitory impulse are transmitted through the autonomic nervous system to the acting tissue cells, this process might be called the "humoroneural regulation of the secretion of the digestive juices." The secretion of saliva is excepted from this regulation.

8. In diabetes mellitus, the same inhibitory and excitatory mechanism is also in force, being different from that in normal cases only in the manner of entrance of these impulses. It is evident from this fact that it is the process of the alternation of hypoglycemia and hyperglycemia that stimulates the excitatory and the inhibitory functions of the secretory centrum and not the durable state of them, which perhaps causes an accommodation such that stimulation is not any longer induced.

9. The humoroneural regulation and the humoral mechanism normally cooperate without interference with each other, an intravenous injection of secretin causing nearly as abundant a secretion of pancreatic juice at the stage of hyperglycemia as at a time of fasting. When hyperglycemia develops, gastric secretion ceases and the entrance of the acid chyme into the duodenum also ceases, so that the secretin mechanism does not have any occasion to function during this period. A hypoglycemia causes a profuse secretion of gastric juice and an abundant gush of acid chyme into the duodenum, which, in turn, induces the full functioning of the secretin mechanism. When, however, a disturbance of gastric secretion occurs, as in achylia gastrica and in cancer of the stomach, the humoroneural regulation alone, without the cooperation of the secretin mechanism, excites the secretory glands of the pancreas to activity.

10. Histamin, a vigorous excitant of the gastric secretion humorally, causes also a profuse secretion of gastric juice at the high point of hyperglycemia. Therefore, it follows that the humoroneural regulation does not have any remarkable influence on the humoral mechanism and this, in turn, proves that the action of histamin does not have anything to do with the neural mechanism.

Concerning the Action of Pancreatic Extracts on Arterial Pressure. — Gley and Kisthinios. (*Paris méd.*, **19** : XI, 93, 1929.)

The authors have shown that a substance can be extracted from the pancreas other than insulin which is positively to be distinguished from insulin and possesses the property of lowering arterial pressure which is demonstrable clinically as well as experimentally. The authors stress the priority of their observation in comparison with other authors.

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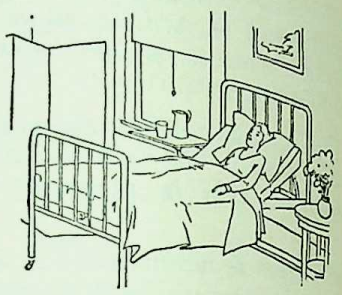
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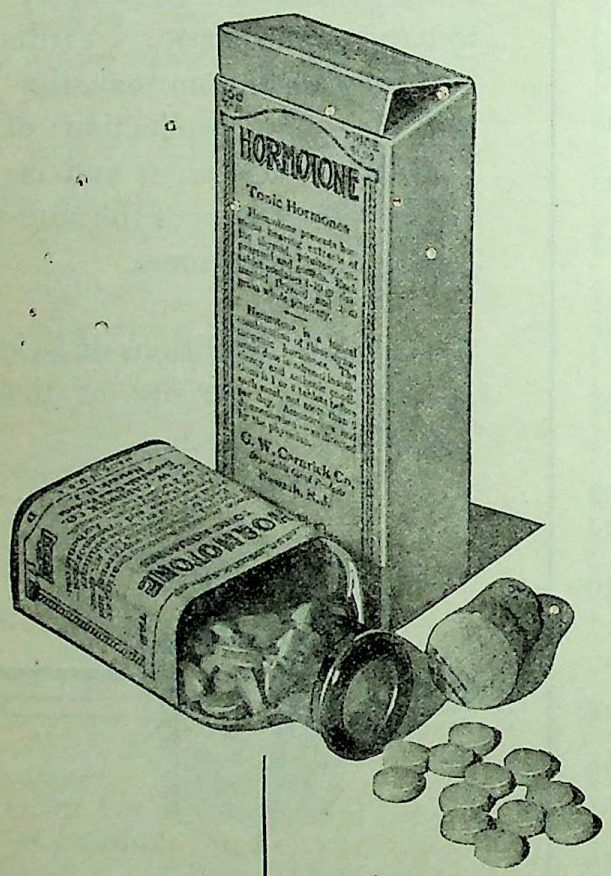
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The Journal of
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The "Heart Hormone" and Heart Beat

THE theory of "heart hormone" as a factor in the maintenance of the rhythm and contraction of the heart is not inconsistent with known facts of the mechanism of the heart beat. All experimental research, however, fails to give evidence of such a hypothetical hormone and, in fact, strongly negatives the theory.

THE tissues and organs of the body which may definitely be classed as endocrine and give rise to internal secretions, the physiological actions of which have been determined, is now fairly well known. It is not a large list and contains a few tissues yet in doubt. Practically every tissue of the body has been suspected of such function and has been investigated.

One of the most interesting attempts has been made to demonstrate the presence of a hormone in the heart. The changed opinion as to the cause of the rhythmic contractions of the heart muscle together with the world-wide interest in physiological endocrine mechanisms made the postulation and "isolation" of a heart hormone almost inevitable.

The description by Remak of that remarkable ganglionic mass in the sinus venosus (sino-auricular node and auriculo-ventricular node in higher animals) led at once to the hypothesis that the mechanism was a nervous one and that the rhythmic stimuli from the ganglionic node, acting as an isolated, automatic nerve center, actuated the heart muscle and gave rise to the regular heart contractions and relaxations. The researches of Gaskell and Engelmann, however, practically forced the abandonment of the theory of nerve control. In the heart of practically all animals

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rhythmic contractions may be maintained when all nerve connection to the sinus venosus is severed and even in isolated strips of heart muscle *in vitro*. The chick heart beats regularly before the development of its nerve cells.

It seemed certain from the above and other evidence of similar nature that the contracting mechanism was resident in the heart muscle cells and the stimulus to contraction might be looked for in some stimulating substance either produced in the cells themselves or brought to them through humoral channels.

The arguments for such a mechanism have more merit than mere enthusiasm for endocrine theories. The neurogenic theory seems definitely untenable. Moreover, the known facts of the mechanism of the heart beat may fairly well be reconciled with a hormone stimulation as the exciting factor. In an adult human heart the centers found in the sinus venosus of the embryo (and lower animal forms) become the *sino-auricular node* and the *auriculo-ventricular node*. From the latter arises a peculiar type of muscle tissue, the bundle of His, made up of primitive, elongated cells (the fibres of Purkinje) which form two main divisions and finally are distributed to the interior surface of the ventricles.

Since the origin of the auriculo-ventricular node lies in the upper part of the heart on the right side at the lower portion of the auricle, there is thus a direct communication between auricles and ventricles. The sino-auricular node, made up of similar tissue, also on the right auricle near the vena cava, initiates the impulses *regulating* the rhythm (but not actually causing the heart muscle contractions). Starting in the sino-auricular node this impulse extends to the auriculo-ventricular node and thus to the ventricles.

But from the standpoint of a theory of hormone control it is important to note that this sino-auricular, auriculo-ventricular mechanism is merely regulatory and that the cause of the rhythmic contractions is inherent in the heart muscle fibre. It has been noted that isolated strips (entirely separated from ne ganglia) of heart muscle may exhibit rhyth contractions for hours. The peculiar rh mic contraction of the heart muscle appears to be related to the stimulus to traction (hormone?) and the nature of the traction itself. The work performed at e contraction is accomplished by the util tion (oxidation) of certain chemical consti ents of the cell and following contraction, relaxation period corresponds to a period new accumulation or formation of compou constituting the "charge" for a new contr tion. This is the "refractory" period of heart cycle. The actual oxygen consump of the heart has been calculated by A. V. H (1).

"The calculated output of blood, multipl by the blood pressure, gives us the work do assuming a mechanical efficiency of 20 p cent, which is a high value under such con tions, the total energy used by the heart c be calculated. The provision of this ener requires the consumption of oxygen, and would appear that the oxygen requirement the heart during such exercise as that describ above is about 300 cc. per minute—abo half its own volume. Assuming a utilisati coefficient of 75 per cent and an oxygen cap city as before, this requires two litres of blo to pass through the coronary vessels of th heart per minute. This volume of oxyg actually used by the heart is almost equal (i gram) to that *required* (*but not obtained*) voluntary muscle during very violent ex cise. The muscle has to stop within a minu owing to oxygen-want; the heart, howev owing to its better oxygen supply, when coronary circulation is efficient, is able to k up an output of this order for long periods. would seem possible that a deciding fac in the capacity of a man for severe prolong exercise may often be the efficiency of coronary circulation."

Stimuli acting during the refractory peri will have no effect because the conditions contraction are not suitable. Now, if a c

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stant minimal stimulus be present, such as a hormone circulating in the fluid tissues, at each heart cycle, when the amount of contractile material is at its maximum, the stimulus of the hormone will release the energy-producing mechanism, contraction will take place and the hormone stimulus will be without effect until there has been a new accumulation of material in the cell. The question as to whether a hormone acts in some way in maintaining the constant and large oxidation in the heart as calculated above by Hill, does not seem to have been investigated.

The theory that a specific hormone is elaborated for the regulation of the heart contraction has been chiefly furthered by L. Haberlandt who, in 1924 (2), stated that he had succeeded in demonstrating a control substance formed in the sinus of the frog's heart and capable of accelerating and strengthening, on the one hand, the automatic impulse of the isolated ventricle, and on the other, of bringing the resting heart cavity to automatic activity. He referred to this stimulant substance as the "sinus hormone" and demonstrated as follows: The pulsating and bleeding sinus is plunged into a small quantity of Ringer's solution and the upper opening of the severed ventricle is at the same time connected with a cannula. This increases the strength of the pulsation and its rapidity. Ringer's solution not so passed through the heart chamber fails to give this result. With a hormone product manufactured from beef hearts, which he later calls a "heart hormone" (3) Haberlandt undertook experiments on the frog's heart. The preparation is also stated to have been clinically successful. The preparation was tested on 36 frog's heart preparations in dilutions of 1-1000, 1-500 and 1-100 with Ringer's solution. With 0.5 cc. of these dilutions the exciting, accelerating and rhythm-producing effects on the heart could be demonstrated. The pulse-exciting effect appeared in 17 experiments and the pulse-accelerating in 26, in 7 of which the automatically pulsating ventricles were first influenced chronotropically and later in the experiment the ventricle which ceased beating was stimulated to renewed action. Such results were also recorded in 7 experiments after removal of the ventricle for a period of 1 day and in 3 experiments after 2 days removal. It was also shown that the "heart hormone" in dilutions of 1-1000 sensitizes the frog's heart ventricle to adrenalin, similar to the effect observed by Demoor and Rijlandt, of aqueous extracts of sinus node on the auricles of warm-blooded animals.

Haberlandt's experiments, despite the fact of the relatively low percentage of positive results (not much more than 50 per cent) and lack of controls, were highly stimulating. Haberlandt's work did not show that the stimulating substance was specific, *i.e.*, whether it was exclusively elaborated in the heart. Subsequent investigations seem to clearly negative this. Rigler and Singer (4) undertook to repeat the experiments of Haberlandt, following the identical procedure under the general direction of Professor Rothberger. They succeeded in demonstrating a stimulating action on the isolated heart, but their positive results as compared with negative were more unfavorable than Haberlandt's. They demonstrated, moreover, that ventricular substance itself (not sino or auriculo node) produced a stimulating substance active in the frog heart apices. They concluded that the stimulating substance is not formed in a specific tissue but in various, widely differing tissues and sites of the body — lower portion of heart ventricle, lungs, liver, spleen and testicles all gave aqueous and alcoholic extracts containing a stimulating substance which can not be distinguished from Haberlandt's, either in its inotropic (affecting the force or energy) or chronotropic action (affecting the rhythm) on the heart or in its solubility or heat stability. Similar substances have also been extracted from the skin (5) and the liver (Asher). Asher (6) in a review of his own work and that of his pupils inclines to the

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opinion that the active constituents of his liver extracts which stimulate the heart are due to cholates. In high dilutions they increase the strength of the heart (inotropic action) and slow the pulse (chronotropic action). In lower concentrations they increase both the strength and the frequency. These results are interesting when we consider the preparation "Eutonin" the "heart hormone" prepared from the liver by G. Zuelzer.

E. D. Oppenheimer (7) also investigated the specificity of this heart stimulating substance. The following tissues were investigated — sino-auricular node, right and left auricles, right and left auricular appendages, right ventricular wall and the base and apex of the left ventricle. Control experiments with tissues other than the heart were made, using striped muscle from the thigh, diaphragm and upper end of the esophagus; smooth muscle from the intestine, stomach and lower end of esophagus, liver, lung and brain. The extracts were made as follows:

"The tissues were obtained from the animal as soon as possible after death, and a weighed amount was ground thoroughly to pulp with a small quantity of Locke's fluid and clean sea-sand. After trituration, the paste was diluted further in the proportion of 1 gram of tissue to 15 cc. (or in later experiments, 10 cc.) of Locke's solution. The mixture was allowed to extract for several hours (generally overnight, for about 18 hours) in a refrigerator, was then centrifuged, and two or more cubic centimeters of the clear fluid used for injection.

"In some cases an alternative extraction was made in a similar way with 95 per cent alcohol. The alcoholic mixture was extracted for 18 hours in a corked flask, was centrifugalized, and the supernatant fluid allowed to evaporate to dryness at room temperature. The residue was then extracted with a quantity of Locke's solution equal in amount to the original alcoholic extract.

"The extracts were warmed exactly to the temperature of the perfusing solution before injection, and were injected slowly so as cause no rise of pressure in the aorta or onary system."

Oppenheimer is in general accord with work of Rigler and Singer (above).

"These results show without doubt there is frequently present in extracts of muscle a substance which has a stimula action upon the beat of the isolated h causing augmentation and often accelera of the beat, and sometimes initiating a in a previously quiescent heart, but o followed by a toxic action.

"The nature of this substance, how appears less certain, as does also the que of its specificity and origin. Accordin Haberlandt (1927) it should be regarded true hormone, which is produced in the s auricular node and other parts of the 'sp musculature' of the heart, and has the spe function of initiating and controlling the h beat. This viewpoint has been rece challenged by many other writers (Rigle Singer, 1927; Rigler and Tieman, 1 Rigler, 1928; Weichardt, 1927; Kisch, 19 and the present research suggests that t doubts are well founded. There is no dence that an extract of sino-auricular is more active than that of other regions the heart; in fact, an extract of the auri (either right or left) usually has a rather strongly augmenting action than that of sino-auricular node. Other parts of the h also, are in many cases equally active, and apex of the ventricle, completely free endocardium to exclude the specialized ducting (Purkinje) cells, may have jus strong an augmenting action as the base.

"In fact, in most experiments the effec extracts of different parts of the hear quite indistinguishable. No support, fore, is obtained from the view that stimulating substance is manufactured in the special musculature, attractive th such a theory undoubtedly is. . . ."

"Taking all these facts into considera it seems doubtful whether one is justifi

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regarding this augmentor substance as a specific hormone, whose function is to initiate and control the heart beat. The fact seems rather to suggest the presence of some product of metabolism in these tissue extracts. Weichardt (1927), indeed, has put forward the view that Haberlandt's 'heart hormone' is merely a particular example of his general hypothesis of the 'function-increasing' action of cleavage products. . . ."

"It appears certain, therefore, that not only is this heart stimulating substance of somewhat inconstant action, and present in only small amounts, but that the special musculature of the heart is by no means the only tissue where it may be found. Whether ultimately it will prove identical with histamine or not, at present the evidence of its specificity as a heart hormone is extremely doubtful."

The evidence of the existence of a heart hormone, arising in a specific tissue and exerting specific effects is incomplete and unconvincing. Heart stimulating substance or substances are found not only in the nodes of the heart but in the heart muscle in which there is no question as to the absence of any specialized tissue. Moreover, these substances may be found in various tissues bearing no type relation to each other. Rigler and his associates have suggested that these substances occur as normal products of body metabolism and exercise this hitherto unsuspected function. They have shown that the substances exert effects similar to histamin on uterine muscle and on blood pressure. Numerous observers have suggested the similarity to histamin in both its pharmacological effects and chemical characteristics. The point of action in the heart mechanism is not clear. Rigler believes that it acts on the anaerobic phase of heart muscle metabolism since the contraction, exciting and strengthening effects may be demonstrated on isolated Purkinje fibres which are believed not to require oxygen in their metabolism. The toxic effects characterizing so many experiments do not inspire confidence in these preparations as containing a true heart hormone. At the present time not only will entirely new evidence have to be submitted but a mass of existing evidence will have to be disproved.

1. Hill, A. V., Muscular Activity, Lectures on the Herter Foundation, Johns Hopkins Medical School, 1924.
2. Haberlandt, L., *Klin. Wochenschr.*, 1924, iii, 1631, Sept. 2.
3. Haberlandt, L., *Med. Klin.*, 1928, xxiv, 22.
4. Rigler, R., and Singer, R., *Klin. Wochenschr.*, 1927, vi, 2357.
5. Weichardt, W., *Klin. Wochenschr.*, 1927, vi, 1555.
6. Asher, *Schweiz. med. Wochenschr.*, 1926, lvi, 1921.
7. Oppenheimer, E. D., *Am. J. Physiol.*, 1929, xc, 656, Nov. 1.

A Contribution to Kottmann's Reaction

(Translated from the article by Dr. Emil Walder, *Mitt. Grenzgeb. Med. u. Chir.*, 1926, 39 : 626, No. 4/5.)

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(CONTINUED FROM VOL. XIV, No. 1)

II. *Clinical Results*

As regards our clinical results with the Kottmann reaction, we may once more stress that the figures noted on our accounts of experiments are no other than degree of browning, which were determined with the as-

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sistance of the standard. In our tables AVBS signifies blood serum from the arm vein and KVBS signifies goiter venous blood serum.

Whether conclusions may be drawn from the greatness of the discrepancy between degree of browning of the arm and goiter venous blood serum concerning the functional state of the thyroid we wish for the time being to leave undecided. We wish merely to note here that in general the goiter venous blood serum shows less marked browning; begins with a lesser degree of browning and sho a slower course of browning, as well in ordina goiters (as may be observed from the follow tables), in cretins (here perhaps most ma edly) as in exophthalmic goiter, where we might properly expect theoretically th the difference would be greatest in exophth mic goiter (reaction error?). A reverse b havior, accordingly, more marked brownin of the goiter venous blood serum than of t venous blood serum from the arm we nev observed.

Table 1. Degree of Browning of Normal Sera

Venous Blood Serum from the Arm (AVBS)

Minutes after Addition of Hydrochinon	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case
0	7	8–9	7–8	7–8	9	8	6
5	7	11	7–8	8	9	10	6-7
10	7–8	11–12	8	9–10	9–10	10	7
15	9	11–12	9	10–11	9–10	11	8
20	9–10	11–12	9–10	10–11	9–10	11	9
25	10	11–12	10	10–11	9–10	12	9
30	10	11–12	10	10–11	9–10	12	9

Table 2. Degree of Browning of Ordinary Goiters

Minutes after Addition of Hydrochinon	Case 1, G. M., 31 yrs. Str. nod. parench. + coll. Pregnancy in 2nd month		Case 2, K. W., 15 yrs. Str. nod. microfoll. and tubul. Basal Metabolism + 5% Rat +		Case 3, W. F., 20 yrs. S diff. coll. Basal Metabo ism + 20% with marke stenosis. Rat 0	
	AVBS	KVBS	AVBS	KVBS	AVBS	KVBS
0	....	....	....	....	....	....
5	8	5–6	6	5–6	5	3-4
10	9	8	11	8	7	5-6
15	9–10	9	11–12	9–10	8	7
20	9–10	9	11–12	10–11	9	8
25	9–10	9	12	11	10	9
30	9–10	9	12	11	10	9

If we consider Table 1, Degree of Browning of Normal Sera, 7 cases, we see that the reaction in these begins with a degree of browning of 7 or 8 and ends with 10 or 11 or 12 (Case 1, 3, 4 and 6). There are also to be sure deviations from this behavior (case 2, 5 and 7). We leave it undecided whether these three cases are dependent upon errors in the method or faulty choice of the normal sera or both together — as much as possible individuals were chosen who were goiter-free, intellectually, psychically and physically n mal. Standard 12 appears to be the upp standard 10 the lower limit for a maxim developed normal serum. Case 7 resembles mild exophthalmic goiter very much, beg with 6+ and ends with 9+, turning brown v slowly.

Cases 2 and 6 appear to stand at the upp limit of the normal sera, where the hyp thyroidism soon begins.

Table 2 shows the results in 3 ordin

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goiters. Among ordinary goiters we understand the cases without clinical symptoms of hypo- or hyperthyroidism, hence physically, psychically and intellectually normal individuals, who are afflicted with a more or less large goiter (condition of euthyroidism).

Case 1 resembles with regard to the Kottmann reaction, a normal serum, perhaps standing on the border towards exophthalmic goiter. Pregnancy in the second month was, however, present; what influence pregnancy has on the result of the Kottmann reaction in the serum, whether direct or via the thyroid, we do not know. It is conceivable that a pregnancy serum assumes exophthalmic goiter like characters as far as the Kottmann reaction is concerned. The goiter venous blood serum distinctly follows after the venous blood serum of the arm in becoming brown as also in the two other cases.

Case 2 is normal according to basal metabolism and rat test. According to Kottmann's reaction the serum resembles a normal serum which stands on the border towards hypothyroidism. The reaction begins to be sure with the low standard degree 6, rises immediately, however, to 11.

Case 3 has a basal metabolism of +20 per cent, probably owing to the marked stenosis of the trachea; no clinical symptoms of hyperthyroidism. Rat test equals 0. Here the Kottmann reaction resembles that of a normal serum, only the reaction begins with a somewhat low degree of browning.

Table 3. Degree of Browning of Exophthalmic Goiter Sera

Minutes Following Addition of Hydrochinon	Case 1. S. A., 40 yrs. Clinically: Basedow. Str. nod. parench. + diff. coll. (Basedowiana). Basal Metabolism + 39.31%. Following ligation of Both Superiores, Basal Metabolism + 9.17%. Rat 0 to +		Case 2. K. O., 31 yrs. Iodin Basedow (Sajodin). Basal Metab. + 47%. Rat ++. Lymphocytosis, 36%	Case 3. L. F., 27 yrs. Pregnancy in 5th Month. Clinically: Hyper- + Hypo-symptoms. Basal Metabolism −1.4%. Rat +. Lymphocytosis 28%	
	AVBS	KVBS	AVBS	AVBS	KVBS
0	5	6	1–2	....	....
5	5–6	6–7	3–4	3–4	2–3
10	5–6	6–7	6	7–8	6–7
15	7	6–7	6–7	8–9	8
20	7–8	6–7	7–8	9	8–9
25	8	6–7	7–8	9+	9−
30	8–9	6–7	7–8	9–10	9−
Minutes Following Addition of Hydrochinon	Case 4. K. C., 25 yrs. Clin. Basedow. Str. diff. parench. (Based.) + Thymus persist. Basal Metabl. + 14.77% +++ Lymphocytosis 48%. 2 Months after Operation: Basal Metab. −6.53%. Rat 0. Significant Subjective Improvement		Case 5. K. Clin. Basedow. Rat +	Case 6. B. F., 12 yrs. Iodin Basedow? Basal Metab. −1.35% or −12.43%. Rat: AVBS + KVBS +	
	AVBS		AVBS	AVBS	KVBS
0	....		6	4–5	4
5	6–7		6	9+	8+
10	7–8		6–7	9–10	9
15	8		7	9–10	9+
20	8–9		7–8	10−	9+
25	8–9		8−	10−	9+
30	8–9		8−	10−	9+
45	9		8−		....

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The degree of browning of exophthalmic goiter sera (6 cases) shows the following relations:

Case 1 concerns a 40 year old patient with Struma nodosa parenchymatosa + diffusa colloides (Basedowiana). Lymphocytosis 41 per cent; basal metabolism +26.87 per cent on the 20th of April, 1923; on the 1st of June, 1923, basal metabolism + 39.31 per cent; on the 2nd of June, ligature of both Aa. thyr. sup.; 2 weeks later on June 15th, basal metabolism +9.17 per cent and rat test with rat reaction to venous blood serum from the arm 0 to +. On August 14th, resection of the goiter and ligation of the Aa. thyr. inf. on both sides. Then, removal of blood for the Kottmann reaction. The browning of the arm venous blood serum corresponds to a moderate to medium degree of exophthalmic goiter, with which gas exchange and rat test harmonize pretty well; the goiter venous blood serum at the beginning of the reaction is about 1 standard degree browner than the arm venous blood serum (reaction error?). The browning increases, however, only about ½ standard degree, so that the arm venous blood serum at the end of the reaction is about 2 standard degrees browner than the goiter venous blood serum.

Case 2 is an iodin Basedow (preliminary treatment with Sajodin) with a basal metabolism of + 47 per cent, rat + +, lymphocytosis 36 per cent. The Kottmann reaction of the venous blood serum from the arm agrees well with this finding and with the clinical picture; begins with 1-2, turns brown relatively slowly and terminates with 7-8.

Case 3 is clinically a mixed case: hypo- + hyper-symptoms in addition to pregnancy in the 5th month. Basal metabolism — 1.4 per cent. Rat +. Lymphocytosis 28 per cent. The browning of the serum is such that one can not decide whether it is a question of a very slight degree of exophthalmic goiter or the influence of pregnancy.

Case 4. Twenty-five year old female patient with clinically distinct exophthalmic goiter, Struma diffusa parenchymatosa (Ba dowiana) + thymus persistence. Ba metabolism + 14.77 per cent, rat test + + Lymphocytosis 48 per cent. Two mon after the operation gas exchange —6.53. P 0. Subjectively, distinct improvement. this the venous blood from the arm sh slight degree of exophthalmic goiter accord to Kottmann.

Case 5. Distinct exophthalmic goite Rat +. Venous blood from the arm accord to Kottmann shows medium degree of exop thalmic goiter.

Case 6. Thirteen year old boy wi questionable iodin exophthalmic goiter. T basal metabolism (—1.35 per cent and —12 per cent at a second determination) spea against it. The rat test: venous blood ser from the arm +; goiter venous blood serum likewise speaks against this diagnosis. the beginning, Kottmann's reaction resembl that of exophthalmic goiter (accident?), r maining course and end reaction behave li normal serum.

It is therefore a question of four clinical sure but mild cases of exophthalmic goit and of two cases whose clinical diagnos was at least doubtful, and which were n hyperthyroid even after basal metaboli and rat test. The exophthalmic goiter cas showed 2 to 3 scale units less browning tha the normal cases; these border cases on th other hand behaved like the latter.

The degree of browning of 6 cretin se showed the following relations:

Cases 1 and 2 concern two sisters, pr nounced dwarf cretins with Struma nodo parenchymatosa + atrophy of the thyr lobe.

Gas exchange, 22.8 per cent or 26.64 per ce
Rat — or —

The Kottmann reaction in venous blo serum from the arm agrees with this. T reaction begins with 10 browning degree increases rapidly and after 30 or 25 minu the browning is more marked than 15. Th

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Table 4. Degree of Browning of Cretin Sera

Minutes after Addition of Hydrochinon	Case 1. B. R., 43 yrs. Dwarf cretin with Str. nod. parench. + Atrophy of the thyroid lobules. Basal Metabl. −22.8%. Rat − −	Case 2. B. E., 48 yrs. Struma nod. Dwarf cretin Gas Exchange − 26.64%. Rat −	Case 3. O. A., 14 yrs. Cretin. Struma nod. parench. lymphocytes 29%	
	AVBS	AVBS	AVBS	KVBS
0	10	10	4–5	4–5
5	11–12	12	6–7	5
10	13	13–14	8–9	6–7
15	13+	14–15	11	9–10
20	14–15	15	11–12	10–11
25	15	More than 15	12	11
30	More than 15	More than 15	13	11–12
45	More than 15	More than 15	13–14	11–12

Minutes after Addition of Hydrochinon	Case 4. J. F., 24 yrs. Cretinoid. Struma nod. parench. microfoll.		Case 5. N. E., 14 yrs. Str. nod. parench. Clin. Cretinism? Lymphocytosis 35.5%. Basal Metab. −5%		Case 6. H. C., 27 yrs. Clin. Distinct Hypo. Basal Metabl. + 7.87% Rat. 0. Str. nod. parench. cyst.	
	AVBS	KVBS	KVBS	KVBS	AVBS	KVBS
0	.....	.....	4	3–4	7–8	7+
5	13	6–7	4–5	3–4	8	7–8
10	13	8	4–5	4	9+	8+
15	13–14	9	5	4–5	9–10	9
20	13–14	10+	7	6–7	10−	9+
25	13–14	10–11	8–9	8–9	10−	9–10
30	13–14	10–11	9+	9	10−	9–10
45	.....	.....	9+	9	10−	9–10

are the most marked degrees of browning which we have ever obtained.

Case 3, clinically youthful cretinism looks like hypothyroidism in the Kottmann reaction also, only the reaction with arm as well as goiter venous blood serum begins with standard 4 to 5 (reaction error?).

In Case 4, mild goitrous cretinism, the serum developed according to Kottmann reaction is again distinctly hypothyroid.

In Case 5 the result of the Kottmann reaction does not absolutely agree with the clinical picture (pronounced cretinism, basal metabolism − 5 per cent, lymphocytosis 35 per cent), since according to Kottmann we would sooner conclude a mild degree of exophthalmic goiter and clinically no symptoms of hyperthyroidism were to be found.

Case 6 is a border case, clinically definite hypothyroid, basal metabolism +7.87 per cent. Rat 0. The Kottmann reaction behaves like a normal serum.

(To be concluded)

Practical Therapeutics

Thyroid Therapy

THE use of thyroid in medicine is based fundamentally upon its remarkable action in increasing the metabolism of body cells. There is no known substance that will exert a comparable stimulus to cell metabolism and it is this definite pharmacologic action that makes it such a valuable

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therapeutic agent. The action is probably catalytic and resembles that of epinephrin, although much more active.

"The physiological action of thyroxine and of epinephrine appear to depend in large part on their effect on processes of oxidation in the animal organism. The weight of material suggests that they act as catalysts. Studies in respiratory metabolism and in oxidation in vitro have afforded an approach to this problem which has already resulted in significant progress." (Kendall-"Thyroxine," 1929.)

The action of thyroid is not specific for any particular type of cell or tissue. Of the several foodstuffs protein fats and carbohydrates all show accelerated oxidation following the administration of thyroid. "The conclusion can be safely drawn that the primary reaction, which is altered by a change in the concentration of thyroxine in the tissues, is intimately associated with an increase in the consumption of oxygen and the output of carbon dioxide" (Kendall).

This non-specific action on cells of all types explains the diversity of therapeutic uses. The article of Oswald (abstracted below) enumerates most of them. In the host of symptoms due to a definite lack of thyroid secretion thyroid gives rise to results little short of astonishing. In infants lack of thyroid hormone gives conditions ranging from a few symptoms referable to the skin and its appendages and slight mental "backwardness" to the marked structural defects, dwarfism and idiocy of fully developed cretinism. It is a question of the degree of the thyroid deficiency, the age and the constitutional type of the patient. In all but the most profound types of mental involvement and in those which have continued for years without treatment, thyroid practically effects a restitution to normal. Even in the marked effect of thyroid on growth there does not seem to be a question of specific effect:—apparently the lack of stimulation to the metabolism of the epiphyses and other growth factors is sufficient to explain the action.

In obesity of various types but particularly endogenous obesity it is usually believed to be effective by reason of its stimulation to greater oxidation of nutritive matter. This is probably the explanation although indirectly it may be related to the storage of foods as glycogen. Thyroid administration lowers the glycogen content of the liver. Hypothyroidism is attended by the same condition. Thyroid stimulates the glycogenic function of the liver and the oxidation of glucose by the cells. It is of undoubted value in several types of obesity, but requires as much care and experience on the part of the physician as the administration of insulin. Oswald's observation that it acts through a dehydrating effect on the organism does not seem particularly convincing. Certainly the effects of thyroid reduction of weight are not comparable to the results of drugs exerting a purely dehydrating effect.

Of greatest interest to general medicine however, is the effect of thyroid in raising metabolism in that class of patients who exhibit generally lowered vitality and lack of energy. The action of thyroid in increasing oxidations and liberation of energy together with its action in increasing the activity of the autonomic nervous system make it a therapeutic agent of unusual value. The autonomic nervous system, through its function of maintaining "tone" of the visceral unstriped muscle fibre, is an excellent way of approach to increasing the "vitality" of the tissues.

A practical point to be considered in thyroid therapy is the delayed action characteristic of this substance. From 6 to 10 days are required to give the maximum effect on basal metabolism. This applies either to injection of pure substance, thyroxin or to the oral administration of desiccated thyroid.

The possibilities of thyroid in therapy have not as yet been realized.

Thyroid Therapy, Its Indications and Contraindications.—A. Oswald. (*Klin. Wochenschr.*, 1926, 5 : 1618.)

In addition to deficiency of the thyroid gland (the complete abolition of its functi-

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there is an insufficiency (a simple decrease of it). On this basis arise the incomplete, partial or mitigated forms of myxedema. In this condition, not infrequently one single symptom surpasses all others and appears especially to be the only abnormal symptom. Indeed, occasionally chronic constipation stands entirely in the foreground and many a case of chronic functional constipation is merely the expression of an hypothyroidism and reacts in a striking manner to thyroid therapy. In other cases, obesity stands in the foreground of the disease picture (thyrogenous obesity). Dietetic treatment is wholly without effect, while thyroid therapy often has an astonishing action. This type of obesity is encountered as well in adults as in children. The pasty, chlorotic, obese types also belong here.

In other cases, the hypothyroidism asserts itself in the form of chronic metrorrhagia with every objectively visible finding lacking in the genital apparatus. Neither the use of styptic remedies nor repeated curetting has results, but thyroid therapy helps in a striking manner. Many cases of pregnancy nephrosis and an edematous tendency of the tissues often appearing in pregnancy are indeed to be conceived of as the expression of hypothyroidism. Here, there appears to be a secondary involvement of the thyroid on the basis of an ovarian insufficiency. In these cases also, does thyroid therapy have a favorable effect. The same would apply for climacteric edema.

Not infrequently manifestations of chronic rheumatism rest upon masked hypothyroidism. That this conception is justified, aside from the therapeutic effect, is shown by the fact that Kocher's "thyreoprivic equivalent" of this type is not infrequently observed following strumectomy. Such cases react especially well to thyroid therapy, defying all other therapy.

At other times, ulcerous dermatitis, among other things in association with localized edema or corpulency, acne, furunculosis, or chronic eczema, is the expression of a hypothyroidism. These cases defy the usual dermatologic methods of treatment, but heal promptly and completely with thyroid administration.

With the above mentioned indications the field of thyroid therapy is not exhausted. Thyroid therapy may be used quite suitably in all cases where one wishes to raise the metabolism and general vital energy. This effect is to be traced back to the beneficial effect proved by experiment, on the oxidation processes and the tonus-increasing action in relation to the visceral nervous system. Thus, Oswald employed thyroid treatment successfully in anemic, asthenic conditions, provided no nervous element was present; in avitaminosis (beriberi), the trophic disturbances are favorably influenced, perhaps through elevation of sympathetic hypotonia. Thyroid medication has also been used effectively to assist callus formation of fractures. This action finds experimental support in the fact that callus formation in the thyroidectomized animal is demonstrably retarded and may be normalized by the administration of thyroid substance. On the other hand, the interesting observation was made that in fractures with the appearance of osteoid tissue in the callus, signs of increased thyroid activity appear in the histological picture of the gland. The application of thyroid preparations supports this action.

Thyroid medication has occasionally a good effect in retarded development which is not of hypothyroid nature, in universal dystrophic infantilism. Also for this effect, must we call upon the metabolism and growth stimulating properties of the thyroid hormone.

Thyroid therapy is a very valuable aid in the treatment of obesity, including obesity of non-thyrogenous origin. Through its well known diuretic property, it serves to dehydrate the organism and at the same time through its property of furthering oxidation, it increases oxidative processes. Self-evident in such cases is the exhortation for caution and for continuous control of the heart.

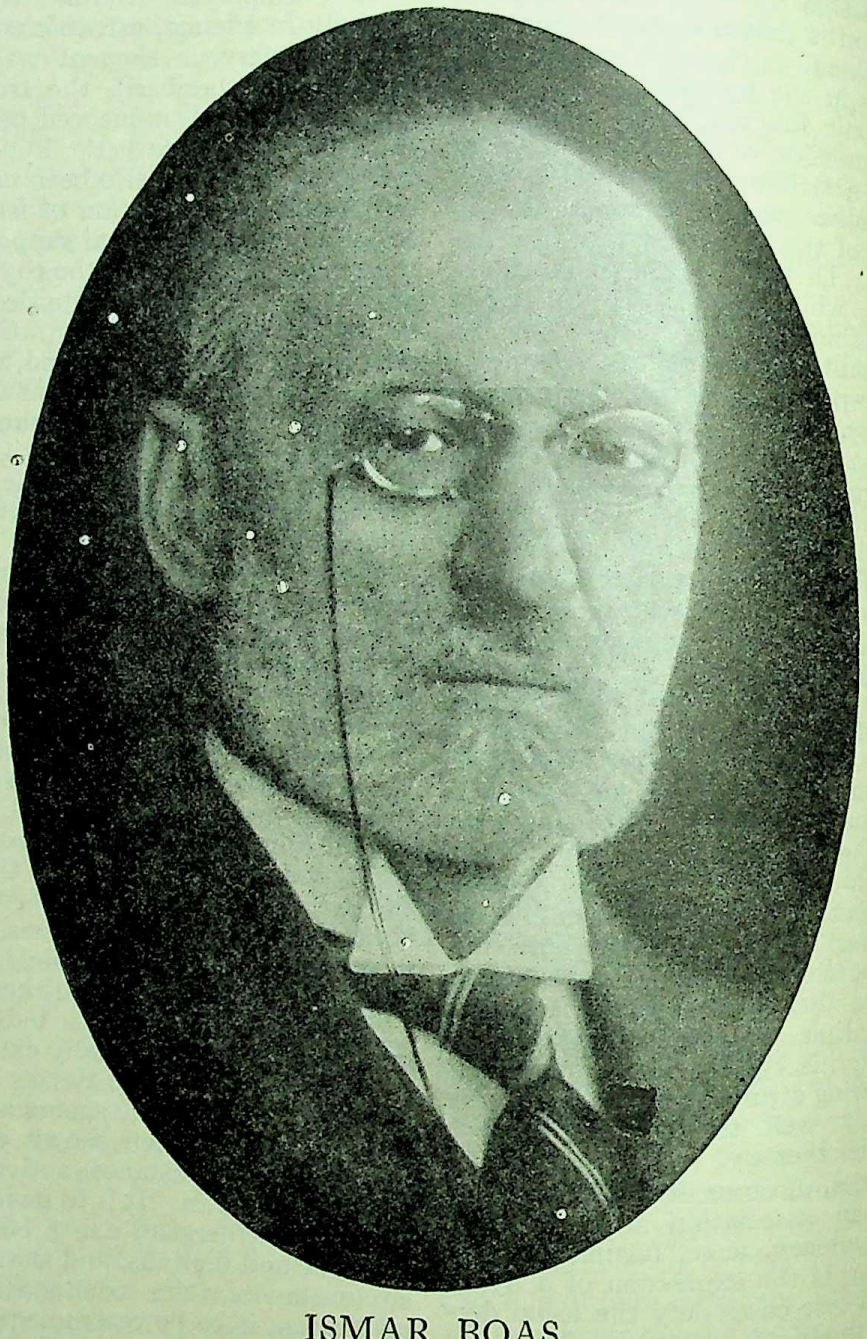
Thyroid therapy is also indicated in genuine nephrosis and in many extrarenally conditioned edemas. The tissues themselves or the intercellular tissue spaces are its point of attack. It has been shown experimentally that thyroid substance activates salt and water metabolism. It is to be mentioned that a positive synergism exists between thyroid hormone and digitalis, and that under certain circumstances, the combination with this medication is to be recommended (Eppinger, Mautner). It appears as if the thyroid hormone strengthens the diuretic effect of digitalis. There are cases in which digitalis fails, where, however, good diuresis occurs, when simultaneous small doses of thyroid preparations are given.

(*Concluded on page 108*)

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The Doctor's Page



ISMAR BOAS
(1858-)

For some scientific workers the name of Ismar Boas may be associated with specialization of gastro-enterology and the founding of the first clinic for the treatment of gastro-intestinal diseases as a separate phase of internal diseases. Others may recall him in connection with an abundance of excellent scientific literature, both in periodical and book form, concerning numerous problems in the gastro-intestinal system: digestion, constip-

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tion, gastric ulcers, gastritis, determination of lactic and hydrochloric acid in the stomach contents, methods of exploring the stomach and its contents. His name is also associated with that of Oppler in the discovery and nomenclature of the lactic acid fermentation bacillus and with several instruments for use in the diagnosis and therapy of gastro-intestinal diseases. Boas' reagent tests for hydrochloric acid and for lactic acid in the stomach are well known. In short, the quantity and quality of Boas' scientific endeavors substantiate the wisdom of his decision to segregate gastro-intestinal from the study of other internal diseases.

Boas' life began in Exin, in Posen, in the western portion of Poland, March 28, 1858, in the large family of a small merchant. The first years of his life were pleasant, for this family was gifted with happy dispositions. The parents wished to give their children a good education, but, unfortunately, the family finances were not abundant, so that it sometimes became a serious problem to pay both the baker and the tutor. However, persistency and a youthful heart helped Boas to face these difficulties valiantly, and meanwhile, to make the most of the little pleasures he was able to obtain while he stored away hard earned knowledge which was to bear ample fruit at some future date.

Boas was sent, with an older brother, to a neighboring *Gymnasium* at Nakel, and then to Züllichau, for preliminary education. In 1877 Boas began the study of Medicine at Berlin, continued it at Halle and completed it at Leipzig where, in 1881, he received the doctorate in Medicine. The dissertation for this occasion concerned the subject of paroxysmal hemoglobinuria, published in *Archiv für klinische Medizin*. It is commended as an excellent clinical study.

Boas was attracted by the experiments, on animals, of C. E. Ewald, Frerich's assistant in Berlin. At the opening of the course of lectures which Ewald was delivering on the subject of physiology of digestion, there were five students enrolled. One by one these dropped out of the class until, at the conclusion, Boas was the sole, faithful survivor. This work was one of the first stimuli to Boas' scientific career, for he was not only interested in the theoretical knowledge obtainable, but he also acted as an experimental subject, himself.

Boas traveled for about a year after graduation, and when he found he was able to do so, he established himself in practice in the environs of Berlin (1882). Then he renewed his former brief association with Ewald, served him as private secretary and assisted in the publication of the *Berliner klinischer Wochenschrift*, of which Ewald took charge at the death of Waldenberg. Later Boas became Ewald's assistant in the Women's Hospital. Here the scientific problems which were ultimately to bring him world fame began to assume proportions. The fundamental experiences for the methods of chemical analysis of the stomach and the succussion experiments were first done at this laboratory. The results of the pathological and physiological findings concerning the digestive system were published in *Virchow's Archiv* (Volume 101, 1885) and in the next year Ewald and Boas contributed further on the same subject (Volume 104, 1886), concerning the lowering of the HCl curve after doses of oil, destruction of ptyalin after high degrees of HCl and the amylolytic and proteolytic stages of gastric digestion.

During the study of literature dealing with the stomach and intestines for this portion of his work, the idea occurred to Boas that this phase of internal diseases was so vast that it might well be segregated for special study, from the rest. He thoroughly convinced himself of the efficacy of this action and then set about establishing himself as a specialist in diseases of the gastro-intestinal tract. Intense disagreement ensued with Ewald, which was never to be entirely bridged over again. Boas' point of view, in the face of the current objections, is well explained in the preface to "Diseases of the Stomach" (1907, translated from the 5th German edition). "Just as the diseases of the nervous system have emancipated themselves from the maternal trunk of internal medicine, without having given up the connection with it, the pathology of diseases of the digestive organs must — if it shall maintain its estate — not by any means lose the connection with the general practice of medicine."

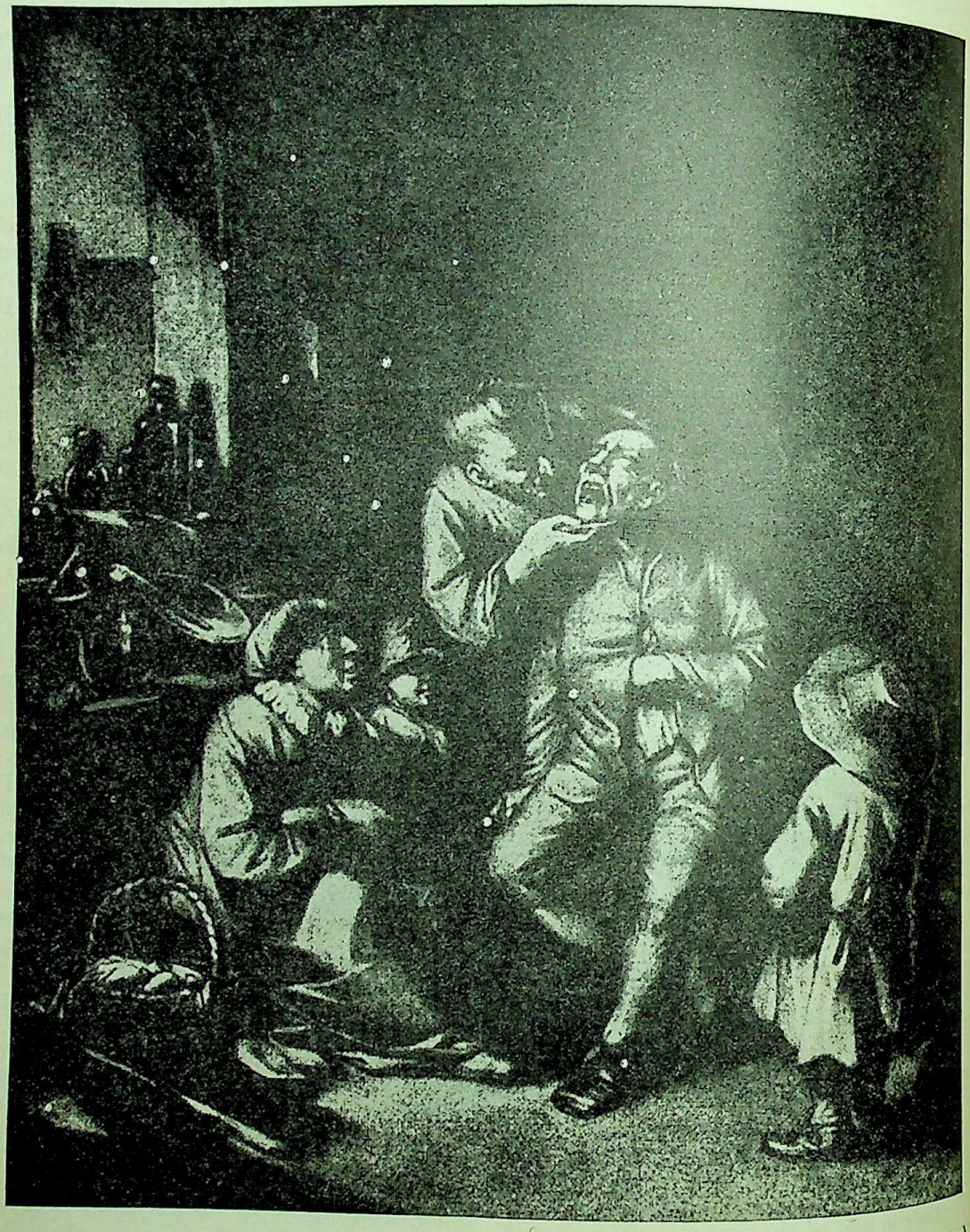
Intent on his own beliefs and disregarding the adverse opinions, Boas founded his clinic for this special study, he gave courses in it which were attended by scores of students of other countries as well as of Germany, and he gave capable young physicians, who attended his classes, opportunities to serve as his assistants. He offered wise counsel; and, with

(*Continued on page 122*)

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Medical Subjects by Famous Masters



"EXAMINING THE MOUTH AND THROAT," by Cornelis Pietersz. Bega (1620-1677)

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Editorial Comment

The Journal of Organotherapy

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Insulin in Non-Diabetic Cases

THE JOURNAL has frequently commented upon the several uses of insulin in cases other than diabetes. Malnutrition, vomiting in infants, in pregnancy and eclampsia, have all been more or less successfully treated with insulin. Schiff (abstract below) discusses the use in ketonemic vomiting in children. He can see no basis for the treatment principally because there is no incontrovertible evidence of an insulin deficiency in children displaying ketonemia and vomiting.

That particular form of acidosis, ketosis or ketonemia, is not only common in diabetes but in childhood as well, and in cyclic vomiting in children there is frequently found large production of keto-acids. There is also a consequent lowering of the alkaline (bicarbonate) reserve. This type of acidosis is usually due to imperfect oxidation of fats — the fatty acids undergoing oxidation until a 4 carbon acid is reached and future oxidation fails at that point. The result is an accumulation of the ketone bodies (beta-oxybutyric acid, diacetic acid and acetone) and an acidosis.

These disturbances in fat metabolism seem to occur in apparently healthy children. There is no question of diabetes or hypoinsulinism present; it is an as yet unexplained phenomenon. It is known, however, that the imperfect oxidation of the fatty acids is almost always accompanied by an imperfect oxidation of carbohydrates. Fats burn in the fire of carbohydrates. Now insulin aids in the oxidation of carbohydrate (sugar) in both diabetic and non-diabetic organisms. It, of course, has other functions, none of which is entirely understood. In the case of accumulation of keto-acids, however, in the blood, the administration of sugar and the concurrent injection of insulin would seem to have a theoretical basis of use by providing an increased burning of sugar which acts as a necessary condition for complete oxidation of the fatty acids. Marriott and Hartman have shown that in the treatment of this type of acidosis in diabetes, the administration of insulin and water is usually sufficient by completely oxidizing the keto-acids and thereby releasing the combined base. This in part restores the lowered alkali of the blood. They found that the concurrent administration of sugar can aid in increasing the keto-acid oxidation and that in great degrees of alkali lowering in the plasma, administration of alkali is effective. Schiff's observation, therefore, that the combined use of sugar and insulin in ketonic vomiting is superfluous, does not seem to be entirely acceptable in the absence of specific proof on this point.

Ketonemic Vomiting and Insulin Therapy. — E. Schiff (*Monatschr. f. Kinderhlkde.*, **42** : 429, 1929).

Favorable therapeutic results were reported by various authors in ketonemic vomiting of children. Without doubt ketonuria in analogy to diabetic coma gave the stimulus to the therapeutic experiments undertaken. Of course, the apparently favorable effect of insulin therapy can only be explained by the fact that the ketones are called forth through lack

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of insulin just as in diabetes. Our knowledge of metabolic pathology up to the present time in ketonemic vomiting is still very inadequate. Yet the little we do know speaks unequivocally against the deficiency of insulin in ketonemic vomiting. In insulin deficiency the carbohydrate utilization in the organism suffers. None of the important symptoms of insulin deficiency are to be observed in ketonemic vomiting of children. The blood sugar is for the most part, if not constantly, considerably lowered. If an analogy can be drawn into consideration, the possibility of a deficiency of insulin in ketonemic vomiting of children is not to be disputed;, the whole symptom complex corresponds to the picture which is observed in overproduction of insulin. Clinical experience as well as experiments undertaken by Hillinger and corroborated by several authors, of a favorable influence of administration of carbohydrate on ketonemic vomiting, also speak against an existing deficiency of insulin. From these considerations the conclusion is given for practical purposes that the sole administration of insulin in ketonemic vomiting is not only unfounded but can also be very dangerous. Kelly reports the case of a child who was brought into a condition threatening life by doses of insulin alone. Frei also states that he is against insulin doses without simultaneous administration of carbohydrate. The favorable reports in the literature are not conclusive since insulin was given simultaneously with sugar. In this combined administration insulin is not harmful, but the injections are a burden to the patient in each case and absolutely superfluous.

Abstracts

Remarks Concerning the Measurement of Insulin. Contribution III. — K. Freudenberg and W. Dirscherl. (*Hoppe-Seylers Zeitschr. physiol. Chem.*, **180** : 212, 1929.)

The authors strove in their experiments for an adjustment between an ideal measurement which takes into consideration the natural conditions of the insulin effect and a measurement which may be technically carried out in the course of an investigation. The authors' measurements showed that one of their laboratory units is the same as 1.8 standard units. According to the opinion of Freudenberg and Dirscherl the crystallizing insulin preparation is the principal bearer of the activity of the technical preparation. They consider insulin as an albumin substance with prosthetic grouping, which is protected by the insulin. If the latter is broken up, then more active preparations of slighter durability may very well occur, as Dingemanse describes them.

Hyperthyroidism and High Blood Pressure. — O. Laufer. (*Med. Klin.*, **25** : 218, 1929.)

The reports concerning thyroid action on conditions of blood pressure in hyperthyrosis are not very numerous but very diverging. The author observed several cases which show that the simultaneous occurrence of hyperfunction of the thyroid and rise of arterial pressure not infrequently is noted. An intimate relationship between both phenomena is assumed although its mechanism in all cases may not be determinable and similar. Even though we have hitherto bestowed consideration predominately on the adrenal system and the sex glands in the discussion of blood pressure conditions, it is shown in such cases that the thyroid and its hormone also acquire considerable significance as hypertonizing factors.

Concerning Treatment of Dysmenorrhea. — W. Liepmann. (*Med. Klin.*, 25 193, 1929.)

The author recommends that each severe case of dysmenorrhea be treated with nasal therapy through application of a cocaine pledget of cotton and that another treatment be tried only when this fails. It is assumed that the diversity of causes also parallels a multiplicity of therapeutic elements and preparations must accordingly be chosen which possess several hormonal components. The author chose a mixture of placenta, corpus luteum, pituitary and ovary and placed especial value on atropin for uterine spasms. Belladonna is used in atropin preparation, a small amount of

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polamin and a small dose of quinine and salipyrin are added. The finished preparation is administered in the form of capsules. Of 20 cases treated in this manner five became entirely free from pain, 12 showed an essential improvement, one case a transient improvement, two cases remained uninfluenced. Among the patients treated, there were 8 women with inflammatory diseases, displacements and processes of involution.

The Results of Treatment by Liver Diet. — K. Heymann. (*Paris méd.*, **19** : 142, 1929.)

The liver extract prepared by Cohn in America contains the anti-anemic factor in almost pure form. The significance of this preparation consists in that chemistry now requires to take just one more stride to produce the active factor in crystallized form. Cohn's extract seems to be almost identical with Seyderhelm's preparation. This is now being used in secondary anemias and has effected a remarkable improvement of the function of the bone marrow. Of course, one question is still unsolved. It is not yet clear whether a detoxicating substance, a hormone or a vitamin factor is introduced with the liver.

Investigation Concerning the Physiology and Pharmacology of the pH on the Heart. — T. Komiyama. (*Naunyn-Schmiedebergs Arch. exp. Path. u. Pharmakol.*, **139** : 100, 1929.)

In the influence of reaction change of the medium on the ventricle, a reversible change of function and an irreversible destruction of the ventricular tissue may be sharply differentiated. The combined action of acids and alkalis with neurotropic bases (adrenalin) behaves analogous to the cooperation of the reaction with the inorganic ions. A strengthening of the positive inotropic adrenalin action through simultaneous rise of the alkalescence could not be reached.

The Injection Method of Transplantation of Endocrine Glands. — H. Küttner. (*Bruns Beitr. z. klin. Chir.*, **145** : 721, 1929.)

The results of transplantation of endocrine glands are not satisfactory since they are only transient and depend on a brief pharmacologic action which expires at the moment when the dying cells are absorbed. The lifetime of the transplant is, to be sure, different and very

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limited in all cases: necroses are always found. Küttner is therefore offering for consideration the injection of living tissue pulp. Kurtzahn and Hübener report concerning objection-free results following injections with thyroid tissues in myxedematous children.

Glycosuria. — F. G. Brathwaite. (*N. Y. State J. Med.*, **28** : 636, June 1, 1928.)

The author made a study of a collection of considerable data made by life insurance companies. This study enabled him to definitely determine that certain groups of applicants with glycosuria, on sub-standard plans, have demonstrated a distinctly increased mortality, and that the greater the quantity of urinary sugar, the higher the mortality.

A study of a smaller but more recent collection of data where the selection is based on other factors than qualitative urinalysis, such as accurate quantitative urinalysis after test meals, and blood sugar determinations, shows that (*A*) Groups of cases have been insured whose mortality was in excess of the expected mortality. (*B*) Groups of cases have been insured whose mortality was less than the expected. (*C*) Groups of cases have been declined insurance who were entitled to it.

Therefore, the author believes that for intelligent study with the view of prognosis in cases of glycosuria, not only must the urine be carefully examined after known test meals, both qualitatively for glucose, acetone and diacetic acid, and quantitatively for glucose (to the exclusion of other sugars), and that comprehensive blood sugar determinations be made both fasting and 1, 2 and 3 hours after the administration of 100 gm. of glucose, or the ingestion of test meals known to contain at least a representative load of carbohydrate. Also, in cases of renal diabetes before an entirely favorable prognosis is given, sufficient consideration must be given to the cause of altered metabolic manifestation as evidenced by (*A*) more or less constant glycosuria, (*B*) eccentricities of "threshold," (*C*) excessive dietary regime, (*D*) overweight, if any or all of these features prevail.

Iodine in Goiter. — William E. Johnston. (*Bull. Wayne Co. Med. Soc.*, **20**: 3, Oct. 2, 1928.)

Prophylactically iodine is indicated in endemic districts to prevent simple goiters during adolescence and to protect the fetus during pregnancy. Therapeutically as a curative agent, iodine is indicated for colloid goiter up to about 25 years of age. It is contraindicated in toxic goiter as a curative agent. Therapeutically as a preparatory agent for surgery iodine is definitely indicated in exophthalmic goiter. It may be used with care as a preparatory agent in toxic adenomatous goiter. Therapeutically as a postoperative agent to combat the induced operative hyperthyroidism and to aid during the convalescence in restoring the thyroid balance to normal.

Oöphorogenic and Psychogenic Uterine Bleeding. — M. R. Robinson. (*N. Y. State J. Med.*, **28** : 1036, Sept. 1, 1928.)

In this paper Robinson considers certain gynecic disorders which are the result of ovarian dysfunctions and abnormal psychic reactions. He says that even this incomplete presentation he gives of the subject suffices to show that the pathogenesis of many types of uterine bleeding resides outside the uterine body, and beyond the confines of cellular pathology. The modern gynecologist in order to serve well, must extend the horizon of his activities beyond the removal of benign or malignant tumors of the generative tract or the salvaging of unaffected remnants left by the ravages of Nisserian, tubercular, or postpartum infections; or the repair of injuries of the generative tract sustained during parturition. The modern gynecologist must go further, he must be trained to recognize functional disturbances as readily as he does organic abnormalities, and from time to time invade the field of the psychologist, for the well being of woman depends as much upon a normal trend of her thoughts as upon a physiologic functioning of the rest of her body.

By oöphorogenic uterine bleeding the author means uterine bleeding in which the uterus as such acts as the end organ through which structural and functional disturbances in the ovary find an outward expression. The effects of these ovarian disorders are first transmitted along afferent sensory nerves of the vegetative system to the spinal nerves, then to the paleëncephalon (especially the pituitary), and from there back again along the efferent motor sympathetic fibers (the hypogastrics) back to the uterus, and the endocrines which stand in close relationship to the generative apparatus. The author gives the following types of uterine bleeding as illustrations: 1. Uterine bleeding in the

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new born. 2. Uterine bleeding in extra-uterine pregnancy. 3. Uterine bleeding associated with microcystic degeneration of the ovaries. 4. Uterine bleeding in cases afflicted with carcinoma of the ovaries.

With the introduction of psychopathology into the realm of gynecology the pathogenesis of many hitherto misunderstood and misinterpreted disorders in the sexual life of women, and in their organs of generation, was placed on a scientific basis.

Function of the Ovary. — Frank A. Pemberton. (*New England J. Med.*, **199** : 87, July 12, 1928.)

Pemberton quotes from Frank as follows: "The function of the adult ovary consists in elaborating a hormone which produces two types of cycles. The one we have called the fertile or complete sex cycle, consisting of maturation of the follicle with its attendant tubular reaction (pregravid reaction), ovulation, impregnation, the elaboration of the corpus luteum, nidation and pregnancy. Pregnancy is attended by the formation of a placenta which in turn sends the female sex hormone into the circulation and assures the continued hyperplasia of the uterus and accessory sex organs throughout pregnancy. Its acme is reached with the onset of labor. The other, called the short, infertile or abortive cycle, does not differ from the fertile one until ovulation has taken place, impregnation for one reason or another having been prevented or not occurring. The corpus luteum then involutes rapidly and therefore the acme of the reaction is reached at estrus in the lower forms or at the time in the human female when the female sex hormone is excreted in the menstrual flow. It is, of course, evident and self-understood that the main, in fact sole, function of the female sex organs is for the perpetuation of the species. To emphasize this function of follicles, corpus luteum and placenta, we call them collectively 'the gestational gland.' "

As Pemberton says, there is some reason for believing that the corpus luteum secretes a substance which prevents menstruation because if a corpus luteum is removed at operation, menstruation appears earlier than it should and if it be done during the early months of pregnancy an abortion frequently follows. As he says, one of the most interesting points, in this work is the possibility, by Frank's method of quantitating the amount of secretion in the blood, or differentiating between amenorrhea due to the absence of the hormone and that due to a persisting corpus luteum. Also in distinguishing various types of menorrhagia or metrorrhagia which may be due to over-production of the sex hormone. Further Frank has proved the sex in two individuals where no palpable uterus or ovaries could be found on examination by demonstrating the female sex hormone in the blood.

Pemberton believes that at present the use of ovarian extracts does not give constant results. There is no unanimity of opinion as to whether the extract of the whole ovary, that of the corpus luteum, or that of the ovary without the corpus luteum is the most effective. These extracts are used for a variety of diseases and at times with success. They appear to be of most use at the menopause, both normal and induced by operation or radium, to relieve the hot flushes and other nervous symptoms. He says that in amenorrhea they are unreliable, one reason being that lack of thyroid secretion and the general health play such a large part in causing amenorrhea. In dysmenorrhea they are sometimes useful in relieving the pain, more often in relieving the nervous symptoms, but rarely give complete comfort. They seem to have little effect in menorrhagia. It is generally conceded that hypodermic administration is more effective than oral.

Novak feels that the results of animal experiments do not throw much light on the human because there is so great a difference in the menstrual function. He thinks that the treatment with ovarian extracts is of most value in hypofunction; that both the follicle and luteal extracts should be used but in a proper sequence simulating the menstrual cycle; and that hypodermic administration is much the surer.

Graves summarizes the use of ovarian therapy as follows: It is a near-specific in the treatment of hot flushes and the vaso-motor disturbances of the menopause. It is ineffective in the treatment of amenorrhea with hypoplasia, menorrhagia, and metrorrhagia. It is occasionally useful in essential dysmenorrhea and the molimenal symptoms of dysmenorrhea. It seems to be beneficial in sterility which might be caused by deficient ovulation. The preparations of the whole ovary or ovarian residue are more efficacious than those of the corpus luteum.

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Cretinism, Diabetes, and Pregnancy. — L. J. Witts. (*Lancet*, **216** : 284, Feb. 9, 1929.)

The case is reported of a woman, 22 years of age, who became pregnant though suffering from cretinism and diabetes. Her mother also suffered from myxedema.

The patient was given thyroid and later insulin and responded well to treatment. She became pregnant. Owing to an oversight insulin was discontinued for 6 weeks when she was readmitted to hospital in coma. Under treatment she came out of coma, the blood and urine became normal, and in a few days she was back on her usual diet. The fetal heart was not heard. Labor commenced spontaneously and she was delivered of a 7-8 months fetus which showed early maceration. Her breasts secreted milk.

Diabetes is more menacing to pregnancy than pregnancy is to diabetes. Conception is infrequent on account of amenorrhea, of vulvitis, vaginitis, and cervicitis, and of voluntary prevention. Before insulin at least 50 per cent of pregnancies ended in miscarriages or stillbirths, and the mother ran a grave risk of coma at delivery, puerperal infection, or aggravation of diabetes. Even with insulin the danger is great. The metabolism is very delicately balanced, and supervision must be close to ensure a normal delivery.

Hypothyroidism is a great, but not an absolute, bar to pregnancy. The occurrence of pregnancy in this girl, who suffered also from diabetes which is inimical to pregnancy, is evidence of the completeness of substitution therapy.

Goiter. — John William Shuman. (*Med. J. and Rec.*, **128** : 339, Oct. 3, 1928.)

The examining physician frequently overlooks goiter as a cause for nervousness, heart disease, loss of weight and other disabilities.

Clinicopathologically goiters are: 1, colloid; 2, adenomatous, and 3, exophthalmic. Colloid goiter occurs in the adolescent, especially at about puberty. The gland is usually enlarged symmetrically and has a soft, velvety feel. Iodine, properly given, is a specific. If not properly managed, this type of goiter is quite likely to give rise to further trouble in the form of adenoma. At puberty, during pregnancy and at the menopause a woman is in danger of a developing goiter. This indicates a close relation between thyroids and gonads. Eighty per cent of pregnant women have enlarged thyroids, which is of no pathological significance. Recent investigations suggest that removal of ovaries causes decrease in size and toxic secretion of thyroid.

There are two types of adenomatous goiter — simple and toxic. The toxic form causes marked symptomatology; the simple is rather a mythical type because it does cause symptoms, although decidedly more mild than the toxic form. "Soldier's heart," the truly irritable heart, is secondary to hyperglandular (thyroid) activity. Many skin lesions yield to the administration of thyroid extract. Obese individuals frequently improve with thyroid feeding but its indiscriminate use in these cases is dangerous. The so-called simple adenomatous goiters are like volcanoes which may erupt on the least provocation. Often an adenomatous goiter undergoes cystic degeneration following the hyperplastic stage. Before goiter surgery became so efficient these were more common. Degenerative myocarditis is a serious result of toxic adenomatous goiter.

Exophthalmic goiter produces exophthalmos, tachycardia, and tremor, in addition to the gland enlargement. Loss of weight, nervousness, insomnia, anorexia, diarrhea and gastric crises may be present. All depend upon the severity and chronicity of the disorder. Patients have been known to have "burned out" exophthalmic goiters, *i. e.*, the disease has ran its course that a cure by nature resulted. This is rare.

With adenomatous goiter the white blood count is usually increased, due to lymphocytosis. The blood pressure is also higher than normal and the left heart enlarged. The metabolic rate is almost always increased but does not reach the high levels so constantly in exophthalmic goiter. Often the two conditions seem present in the same individual and microscopic sections often show adenomatous glands with hyperplasia.

Practically the only difference is the presence or absence of exophthalmos, and definite adenomatous areas in the gland. The history of the case is of diagnostic significance. A goiter which has been present for a number of years and is suddenly productive of toxic symptoms, is almost certainly a toxic adenoma. Treatment of toxic adenoma is always surgical; of exophthalmic, medical followed by surgical; administration of Lugol's solution is of value in the exophthalmic type. Lugol's solution should be used with great

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care, only in preparation for operation, and then started 2 weeks before; after this it loses effectiveness. It is contraindicated in toxic adenoma because many simple adenomas have been changed to toxic adenomas by the indiscriminate use of iodin.

Benign Hemorrhages of the Uterus. — Henry Schmitz. (*J. Am. Med. Assn.*, **91** : 955, Sept. 29, 1928.)

Uterine hemorrhage is one of the most important clinical signs of diseases of women. The causative, functional and pathologic disturbances are of equal importance, as the indications for treatment and the methods employed should be based on them. This presentation of the subject comprises: (1) the classification, etiology and frequency of uterine hemorrhages based on pathologic physiology and anatomy, and (2) the treatment of benign uterine hemorrhages due to functional disturbances of the uterus and ovaries. The study is based on a survey of 2184 consecutive hospital records and 2126 records of outpatients. The number of benign uterine hemorrhages in this series was about 25 per cent of the total cases admitted. The classification and frequency of the types of bleedings was:

(*a*) Hyperemia: The menstrual flow lasts too long or is too profuse. It is due to uterine dysfunction. The frequency is about 60 per cent of the total benign hemorrhages.

(*b*) Polymenorrhea: The menstrual flow occurs too soon. It is caused by ovarian dysfunction. The frequency is about 20 per cent of the total benign hemorrhages.

(*c*) Metrorrhagia: There is a bleeding independent of the menstrual flow. It is the result of the loss of continuity of the surface epithelium by ulceration, necrosis or rupture of proliferating processes within the genital canal. The frequency of the benign metrorrhagias is about 20 per cent of the total benign hemorrhages.

A diagnostic curettage and microscopic examination of all scrapings are necessary in those cases in which (1) a correct diagnosis by physical examination can not be made, and (2) the hemorrhage occurred in the menopausal period of life. A woman suffering from a uterine hemorrhage should not be treated until the underlying cause has been determined. All uterine bleeding must be viewed with grave suspicion until it has been proved to be benign. In the treatment of benign uterine hemorrhages due to functional disturbances the age of the patient must be considered, the cause removed, and normal function of uterus and ovaries reëstablished, if at all possible.

The contractility of the uterus is stimulated by ergot, hydrastis, extract of the posterior lobe of the pituitary gland and epinephrin. Ovarian dysfunction indicates extract of the anterior lobe of the pituitary, thyroid, the ovarian follicle and the corpus luteum. The removal of the true corpus luteum causes death of the ovum and abortion. Hence the life expectancy of the non-impregnated ovum depends on the corpus luteum. The endocrine extracts should be given hypodermically. Their action is a problematic one, as uniformly good results are not often seen. General management of each case is important.

The menopausal benign bleeding may be treated less conservatively.

Radiation therapy was indicated in 32.31 per cent of the benign functional hemorrhages and 11.03 per cent of uterine myomas.

Relation Between Gall-Bladder Disease and Pancreatitis. — Daniel Fiske Jones. (*New England J. Med.*, **199** : 716, Oct. 11, 1928.)

The frequency of the association of gall-bladder disease and pancreatitis has been estimated at from 20 per cent to 50 per cent, and careful routine examination, as carried out at present, of the pancreas and gall bladder may give a still higher percentage. The great increase in the number of so-called chronic cholecystitis cases is believed by many to be a serious condition that may lead to pancreatitis and many other conditions.

The writer, in this paper, endeavors to set forth clearly some of the clinical and pathological features of what appears to him to be two entirely different types of pancreatitis: 1. Acute hemorrhagic pancreatitis. 2. Cases where the patient has frequently had previous attacks of gall-stone colic, or cholecystitis; he is usually operated upon for gall-bladder disease.

The author believes that gall stones should be removed with the gall bladder when found, if there are no contraindications. He has seen no evidence whatever to prove that the cases of so-called chronic cholecystitis, in which no gross pathology can be demonstrated, and the cholesterol gall bladders have any causative relationship to acute hemorrhagic

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pancreatitis, and if these gall bladders are to be removed, it must be done for some other reason than the prevention and cure of acute pancreatitis. He believes, considering all known facts, that the treatment of chronic pancreatitis should be to remove any source of infection and drain the biliary system. In acute hemorrhagic pancreatitis Archibald's theory should serve as a guide, and drainage of the biliary system established by cholecystotomy, cholecystectomy and drainage of the common duct, or by cutting the sphincter of Oddi. In addition, he believes that the capsule of the pancreas and fatty capsule should be drained.

Emotional Polycythemia. — J. J. Izquierdo and W. B. Cannon. (*Am. J. Physiol.*, 84 : 545, Apr., 1928.)

Emotional excitement (of a cat in the presence of a dog), for 1 minute, is quickly followed by a pronounced increase of the red corpuscles of the blood. In 15 observations of increases below 30 per cent the average increase was 20 per cent. The increases are far beyond the variations occurring in the usual quiet existence of the animal. The maximal increase is immediately after the minute of excitement; after 5 minutes a fall has started; and within a half-hour the former state has been restored. If the conditions which usually cause excitement fail to do so, the polycythemia does not occur.

Hematocrit and hemoglobin determinations do not show such great increases as does the erythrocyte count; this is explained by a larger percentage of small corpuscles in the blood after excitement.

Emotional polycythemia fails to occur after removal of the upper abdominal sympathetic strands and bilateral severance of the splanchnic nerves. It may even be replaced by a lower erythrocyte count. If only the liver among the upper abdominal viscera is left innervated, excitement causes no noteworthy hyperglobulia. After section of the nerves to the spleen excitement for one minute does not produce polycythemia; prolonged excitement with struggle may occasionally increase the erythrocyte count.

The above research was undertaken to determine, if possible, whether the spleen, instead of the liver, might be the source of emotional polycythemia. The authors ask — do the adrenal glands play an essential rôle? If not, do they play any rôle — are they capable of producing any effect on the corpuscular content of the blood? In the experiments the adrenal glands were active. An irregular effect of secreted adrenin and of injected adrenalin are attributed to variable concentration of the blood in the denervated spleen. Inactivation of the adrenal medulla was found to have no marked influence on emotional polycythemia.

From their studies the authors conclude that the liver is not a significant factor in emotional hyperglobulia. Evidently the spleen is the immediate cause of polycythemia.

Dextrose-Insulin Treatment of Shock. — Preston A. Wade. (*J. Am. Med. Assn.*, 90 : 1859, June 9, 1928.)

The author found that dextrose administered intravenously with insulin subcutaneously in cases of shock gave results more satisfactory than could be obtained in cases treated by saline or dextrose solution alone. Cases of traumatic shock treated early responded most readily to this treatment. Cases of post-operative shock treated in this manner showed marked improvement.

The optimal dosage is 1000 cc. of 5 or 10 per cent dextrose with 1 unit of insulin to 3 gm. of dextrose. Beneficial results are usually apparent after 800 cc. of fluid has been injected. Cases of shock in which the blood pressure is decreasing toward the "critical level" (80 to 90) should be treated immediately before the rapid fall which usually follows with symptoms of severe shock.

The Embryohormonic Relations of the Suprarenal Cortex to Mesothelial Tissues. — Robert C. Moehlig. (*Ann. Int. Med.*, 1 : 828, Apr., 1928.)

The object of this paper is to show that the suprarenal cortex secretion has a selective action on mesothelial tissues. The important mesothelial tissues, sex glands and skeletal muscle are influenced by the state of the suprarenal cortex. Both the mesenchyme and the allied mesothelium through the suprarenal cortex are influenced by the pituitary gland.

Undescended Testicle. — Herbert W. Meyer. (*Surg., Gynecol. and Obstet.*, 44 : 3 Jan., 1927.)

The exact etiology of undescended and ectopic testicle has not yet been definitely settled. The histological changes point to

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fact that spermatogenic cells are present and functionate in about 10 per cent of all cases. The interstitial cells, which have to do with the development of the secondary sexual characteristics, are always abundantly present. These findings are almost constant, and therefore, the undescended testicles should always be saved.

Secondary complications occur. Malignant degeneration is not as frequent as is generally supposed. Fear of this is no indication for orchiectomy. Chronic inflammation, the presence of a potential or real concomitant hernia, practically always present, torsion of the spermatic cord, and strangulation of the testicle, are occurrences so frequent that surgical interference is always indicated. Pain is the most frequent symptom. In adults psychic disturbances may occur on account of the depression that comes from the knowledge and fear of abnormal sexuality.

The best time for operation is before puberty, between 8 and 10 years of age in patients with unilateral undescended testicle, and earlier in bilateral cases.

Histological Study of the Thyroid of the Guinea Pig in Experimental Scurvy. —Katherine D. Harris and Erma A. Smith. (*Am. J. Physiol.*, **84** : 599, Apr., 1928.)

As a result of scurvy the thyroid gland shows an increased amount of interfollicular cells, a decrease in colloid, an increase in the number of vacuoles, and a lengthening of the cells lining the follicles, the degree of change depending on the length of time the animals survive the scurvy-producing diet. Acute starvation of guinea pigs reveals no changes in the thyroid by the present method. The results are interpreted as an indication of pathology in the thyroid as a consequence of vitamin C deficiency.

Cod Liver Oil in Parathyroid Tetany. — John C. Brougher. (*Am. J. Physiol.*, **84** : 583, Apr., 1928.)

The addition of cod liver oil to a mixed stock diet for thyro-parathyroidectomized dogs delayed the onset of tetany and lessened its severity when it did occur.

Serum calcium in control and in test animals dropped to the tetanic level but tended to approximate the normal in 30 to 40 days in the animals given cod liver oil.

The point is further confirmed that low serum calcium is not always accompanied by tetany. Cod liver oil relieves tetany and benefits parathyroidectomized dogs either by improving calcium absorption, mobilizing body calcium, or increasing the ratio of ionized to unionized calcium. Thyro-parathyroidectomized animals have been carried through estrus, pregnancy and lactation by the addition of cod liver oil to the stock diet.

The Climacterium in Males. — H. Lyons Hunt. (*Med. Times*, **55** : 75, Apr., 1927.)

The ebb of sexual activity and a critical period of life is common to man as well as woman. Facts prove that the secretion of semen diminishes greatly in quantity as well as in its fecundating power, at about the age of 60. Exceptions are on record of men whose procreative power has been prolonged to the age of 90 or 100, but these cases are exceptional.

There are pathological changes which have been termed "climacteric diseases." Paul asserts that prostatic enlargement in advanced life is the result of an involution change comparable with involution hypertrophy of the breast of the female at the climacteric period. Investigation has led to the belief that all activities of the body — muscular, glandular and visceral — are controlled and regulated by the nervous system. It has been assumed that the ductless glands and their internal secretions play an important part in sustaining the equilibrium of metabolism. The gonads have an internal secretion which acts upon the metabolism to stimulate it in each sex in a specific manner.

There has been too much confusion in speaking of the sex life of man. It is invariably referred to in a general way to include under one heading various phases, namely, sex desire, potency and virility. Until each of these conditions is taken up as an individual entity, the confusion will persist. Each one of these conditions may be present or absent without marked relationship to each other. Hunt cites cases which illustrate this. Also, it is known that there are cases where the testicles and the prostate are normal, but the posterior portion of the pituitary gland becomes involved pathologically and an impotence develops. In association with many pathological conditions, impotency may develop; also, loss of sex desire, loss of virility develop, and yet the testes and prostate remain anatomically unaltered. During the

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climacterium acute and chronic diseases are attended with more than the usual dangers because the powers of resistance are less competent then to battle with the infective or toxic invasion.

Certain climacteric diseases stand out on account of their frequency. Arteriosclerosis is to be regarded as physiologic in a man past 60, though there are certain factors which hasten its development, such as syphilis, infectious diseases, rheumatism and gout. Aortic arteriosclerosis is the most frequent of the arterial degenerations occurring during the climacteric. Just what relation arteriosclerosis has to the endocrine glands is not known. In a series of four hundred cases of transplantation which Hunt performed were a number of cases of arteriosclerosis associated with high blood pressure. He cites cases in illustration. Following transplantation the blood pressure dropped to almost or quite normal where it remained until the transplanted tissue began to be absorbed when it started to rise. This has also been the experience of Stanley and Voronoff. The earliest cardiac change is a cardiac hypertrophy. The chronic endocarditis which is frequently seen in the male climacterium is simply part of the arteriosclerosis of this period. Among other so-called preferential diseases is cancer, which, according to Cohnheim's theory, arises from faulty embryonic development, embryonic cells remaining dormant until later life. The frequency of cancer at this time would strongly suggest an endocrine basis for these abnormal cells, or, at least, the malignant cells receive a nourishment from the abnormal chemicals which are floating in the blood stream at this period. It is known that grafting of cancer cells is not successful in young rodents, but cancer grows with avidity if cells are grafted from one ageing rat to another. It is also known that in gonadal transplantation experiments on rodents, organs which appeared shrivelled and aged will take on the appearance of youth and health within several weeks of a transplantation.

All the climacteric diseases, whatever their nature, are the manifest symptoms of the failure of some governing power regulating the organic processes, and are, as far as present knowledge goes, connected with the dysfunction of the glands of internal secretion. All the physiological changes mentioned by Hunt can be artificially produced. When this is done they occur in a much more aggravated form. Many of the organic disturbances occurring during the climacteric virile are to be regarded as physiologic processes, which, under certain circumstances become pathologic. Many authorities ascribe a deeper significance and greater seriousness to physical deteriorations incident to the male climacterium than to those observed during the menopause, because the death rate of man is in such an extraordinary excess over that of woman at the menopause period. More serious than the physical changes, however, are the mental disorders which may manifest themselves during and after the male climacteric. Loss of memory, loss of self-control often leading to hysterical and emotional conditions, neurasthenia, anxiety neurosis, incapability of concentration, hypochondriasis and suicidal impulses may develop during this period. There may be introspection, with natural fears and unnatural phobias. As a rule the libido, and also potency, decreases, though sometimes there may be a considerably increased libido. Climacteric men often complain of disturbances during coitus, such as orgasm without ejaculation, ejaculation without orgasm, ejaculatio precox, or ejaculatio deficiens. The most distressing manifestation of the climacterium virile are deviations from the normal vita sexualis. Frequency of sexual perversions are greater after puberty than before. This frequency increases with advancing years. The frequency with which climacteric men plunge into sexual debauchery and commit erotic follies challenges the profession to search for an underlying physical cause for such conduct. Lydston advances the theory of a perversion in the quality and quantity of the endocrine secretions, and that the point of departure is to be found in the testicular cells of Ledig, with an aberration of the sex hormone. The vicious circle once established, all of the endocrine secretions play their part.

While Hunt, as a result of his experience, believes implantation of gonadal tissue to be the most logical treatment for disease during the climacteric period and due to the changes taking place at that time, he does not believe nor contend that transplanted gonadal tissue is a true transplantation, but is a transplantation of tissue which is going to be absorbed in a short time. It may last a few months to a year or a little longer, depend-

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on the condition of the patient, and in some cases will have to be repeated if the good results are to persist. When gonadal tissue is transplanted, the operator transplants gonadal tissue, composed of thousands of endocrine-producing cells, endocrines which are deficient, especially at the climacteric period of life. During the absorption of this tissue, these endocrines are also absorbed, and supply the body with that which is most vital and necessary to prevent the depredations that the patient is undergoing from their deficiency.

Further Contribution on the Question of the Variability of Hormone Action. — Electrodialysis and Insulin. — H. Zondek and H. Ucko. (*Klin. Wochenschr.*, **5** : 1861, 1926.)

Statement of the theory of the method. Insulin loses its normal activity through electrodialysis. It is also possible for it to lose completely its blood-sugar lowering activity, although there can appear qualitative changes in its type of action. Thus the authors in a series of trials observed that a demonstrable, insignificant and transient decrease in blood sugar followed a relatively marked rise of blood sugar. Also in the experiments in which the blood sugar lowering effect was completely preserved, after 2 to 3 hours, following the injection, there appeared a rise in blood sugar.

The question concerning the manner in which the profound change in insulin action takes place, can of course scarcely be answered with certainty. Our first thought will be of physical surroundings within the insulin molecule, somewhat in the sense recently accepted by Kendall for thyroxin under certain circumstances. The authors believe that for the purpose of regulation of its biological reactions, especially of the physiological term of cell functions, not alone the means for alteration of the colloid condition of the cell is at the disposal of the organism, but that here also the modification of the secretion acting on the cell, in structural as well as biological relations, enters the problem. This point of view should also be significant for clinical pathology. Thus, it is known that there are a number of diabetics who remain refractory to insulin. On the basis of the author's investigations, this need not be especially surprising. Slight anomalies of the colloid condition of the cell, the most delicate disturbances of the osmotic and electrical forces playing on the cells of the organ affected, are sufficient to transform the efficacy of the secretion or preserve it, even when it is formed in sufficient amounts in the organism or given up to therapeutic uses.

Hematuria During Treatment with Insulin. — A. V. Neale. (*British Med. J.*, **3531** : 442, Sept. 8, 1928.)

Because of the rarity of hematuria occurring in diabetic patients under insulin treatment Neale reports a case in which it occurred in a boy aged 5 years.

The points of interest peculiar in this case are: (*a*) that the hematuria was extreme but of very short duration; (*b*) the rapid return of the urine to the normal; (*c*) the hematuria occurred 2 days after the last dose of insulin; (*d*) there was at this time only a slight ketosis.

Clinically this case did not appear to be one of nephritis. The benign nature of this urinary abnormality was apparent in this case and is in accord with observations made in other cases by Lawrence.

Concerning the Thyroid Function Following Removal of Goiter. — B. Breitner, E. Nobel and A. Rosenblüth. (*Mitt. Grenzgeb. Med. u. Chir.*, **39** : 45, 1926.)

Follow-up investigations on 32 cases, in which in the last 3 years owing to impediment to breathing only resection of the goiter was carried out, were made by means of Krogh's apparatus. The result may, therefore, be summed up in the statement that following extensive resection of goiter with a good operative technique, signs of decrease in function in the sense of a hypothyroidism are not to be feared.

On the Activity of the Posterior Lobe of Human Pituitary. — W. Lampe. (*Arch. exp. Path. u. Pharmacol.*, **115** : 277, 1926.)

In order to investigate the activity of human pituitary glands, these were removed shortly after death, the posterior lobe cut up in acetone and preserved on ice. On the next morning, the remaining acetone was removed, and the pituitary left in the exsiccator for 24 hours at 37°. On the third day the pituitary preparation, by this time already considerably dehydrated and defatted, was extracted for 3 hours with acetone in a Soxhlet apparatus. For the production of an

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extract the substance was then pulverized after evaporation of the acetone, in the agate mortar, dried for 24 hours in the exsiccator and then 1 cc. of 0.25 per cent acetic acid added per mg. of substance. The average weight of 20 human pituitary posterior lobes amounted to 0.11 gm., the yield 12.3 mg., therefore, about 11.5 per thousand. The blood pressure effect was tested on cats. An elevation of 10 mm. Hg was regarded as stimulation threshold. The still active amount oscillated between 0.01 and 0.2 mg. desiccated substance.

The antidiuretic effect was investigated on dogs with urinary fistulae in accordance with the well known method of Kestranek, Molitor and Pick. The still active dose with antidiuretic effect lay between 0.025 and 3 mg. desiccated substance. The uterus effect was tested on isolated guinea-pig uterus. 1:2 millions to 1:700 millions (referred to dried substance) was shown to be the effective marginal concentration.

The results of investigation yield therefore an extraordinary variation in active substance in the pituitary. The pituitary seems to be very resistant to external influences. The activity of the extract bore no relation to the time which elapsed between death and the removal of the pituitary (from 3½ to 27 hours after death, removal had taken place). The antidiuretic and uterotonic effect always paralleled the individual preparations. It could not be determined what relations there were between activity and the different diseases which the patients succumbed to. It was noteworthy, however, that an active preparation was derived from one woman who had been castrated years before.

The Clinical Value of Interferometric Blood Analysis in Polyglandular Endocrine Disturbances Especially for the Significance of Psychic and Constitutional Anomalies. — F. M. Groedel and G. Hubert. (*Münch. med. Wochenschr.*, **73** : 1738, 1926.)

Through the interferometric blood analysis by Paul Hirsch's method we have succeeded in ascertaining quantitatively to a positive degree the organic break-down of each gland and in deducing from the figures obtained the functional disturbance in particular and the degree of the functional disturbance. This method held good in endogenous obesity and the thyrogenous diseases. This condition induced the authors to employ the method in cases in which they considered the so-called constitutional anomalies as a sequel to internal secretory disturbances, in the expectation of ascertaining the actual functional disturbance from the quantitatively different organ decomposition values. Among other things they also succeeded in actually showing that slight psychic disturbances, to be inserted clinically into no disease group, accompanied similar changes in the internal secretions.

Among others, the authors describe the case of a mother and daughter. The mother showed mild psychopathic characteristics. Palpable clinical deviations were lacking. The patient gave the impression of a constitutionally inferior personality, probably consequent to disturbances of the internal secretions. The interferometric blood curve showed very clearly that this suspicion was correct. It showed a quite extreme functional disturbance of the thymus. Obviously, this organ persisted owing to excessive hypofunction of the ovary, and was hyperplastic. Whereas, otherwise, from the high decomposition value of one gland one would infer a hypofunction resulting from a disease change of this gland, and the disintegration of cells resulting therefrom, here one must infer increased cellular disintegration through diseased and abnormally increased glandular activity (pituitary) and from the slight decomposition value of the antagonistic gland (ovary), the hypofunction of which is the basis of a hypoplasia. To this correspond the assertion that the menses are always quite weak and of short duration. Furthermore, in such cases, the increased decomposition for testicle in women is interesting and significant, often a sign of a virile sexual type. *Vice versa*, one also sees in men with feminine inclusions, an elevated decomposition for ovary.

The 12½ year old daughter is very nervous and has not yet menstruated. One has the impression of a psycholability with depressive characteristics. The interferometric curve showed in contrast to the curve of the mother a clearly increased ovarian decomposition value. In the daughter's case, also, however, the testicular decomposition outweighed in the expression of a virile type. For the reason the cause for the constitutional psychasthenia is to be sought in all probability in disorders of internal secretion.

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If the postulations of the investigators should be corroborated in a great series of investigations, then there would perhaps be found in organotherapy in this field, a rich prospect for the removal of these psychic disturbances.

Pluriglandular Instability Resembling Aborted Form of Exophthalmic Goiter. — Léopold-Lévi. (*Presse méd.*, **35** : 56, Jan. 12, 1927.)

The patient showed signs of aborted exophthalmic goiter, including the ocular symptoms. More exact endocrine examination revealed thyroid instability and suprarenal insufficiency. The whole symptom complex was transformed by suprarenal organotherapy. In this respect, the author studied the importance of basal metabolism, which was decreased in this case; the relationship of this syndrome to tuberculosis and syphilis; the antisyphilitic treatments; the importance of Bouchard's nodules, and of gastroptosis in the exteriorization of congenital suprarenal insufficiency.

Interferometric Investigation of the Endocrine Exhaustion during Pregnancy under Normal and Pathological Conditions (Eclampsia and Hyperemesis Gravidarum). — Hellmuth. (*Deut. med. Wochenschr.*, **52** : 1892, 1926.)

Through the nidation of the fertilized ovum changes exist in the maternal organism quite early, in which, on the basis of recent results of research, the glands with internal secretion take part regularly and legitimately. In order to draw attention briefly to the most important changes in the endocrine glands during pregnancy, the author recalls the already externally visible enlargement of the thyroid in many cases, the typical changes in the pituitary, the broadening of the suprarenal cortex as well as the changes in the ovary which in the beginning of pregnancy lead to cessation of follicular ripening. It appeared therefore to be relevant to undertake investigations to ascertain whether the interferometric method was in a position to give new glimpses in this field.

Diseases of endocrine origin present a very important field for the application of the interferometric method. Since, according to the state of present day research, during pregnancy there is regularly concerned in almost all the endocrine glands a functional increase in the sense of an increased functional glandular activity, an abnormally high endocrine exhaustion is *a priori* to be expected in the interferometric investigation. The investigations of the author have extended to the behavior of the following endocrine organs: thyroid, pituitary, suprarenals, pancreas, ovary, testicle, placenta, as well as incidentally also the thymus and pineal gland. The result of interferometric investigations of this kind was, however, negative, despite the fact that in pregnancy and childbirth in most cases an actual increase of endocrine function is concerned. This result stands in accord with the experiences which the author has collected with interferometry in disease conditions modified by the endocrine glands outside of the gestation period.

Complete Arrhythmia, Cardiac Insufficiency and the Thyroid Gland. Deductions from Medical and Surgical Therapeutics. — C. Lian, L. Lyon-Caen and L. Pollet. (*Presse med.*, **35** : 33, Jan. 8, 1927.)

Various cardiovascular disorders are observed in the course of thyroid affections: cardiac insufficiency and various changes in cardiac rhythm, in particular, complete arrhythmia, which frequently arises in exophthalmic goiter. The authors reviewed all the cases of exophthalmic goiter collected by one of them for the past 15 years (comprising cases of confirmed exophthalmic goiter and toxic adenoma), omitting the cases of aborted exophthalmic goiter. Complete arrhythmia was encountered quite often in these cases, in a proportion of approximately 10 per cent of the cases; but it was not the usual finding. Relative to the frequency with which this symptom was noted in exophthalmic goiter and in toxic adenoma, it appeared to be slightly more frequent in the latter group. The authors also noted that complete arrhythmia in cases of goiter without hyperthyroidism is far from being an exceptional finding.

The pathogenesis of complete arrhythmia in exophthalmic goiter is still under discussion. Today, the tendency seems more and more toward giving to the toxic factor the preponderant rôle. The intoxication seems not only to be the principal cause of Basedowian asystole, but of disorders of cardiac rhythm in Basedowians as well.

These conceptions show that the therapy of complete arrhythmia in exophthalmic goiter should be directed principally against the

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thyroid disease and secondarily against the arrhythmia itself. The underlying treatment of dysthyroidism may be medical or surgical. In accord with the opinion of many others, the authors believe that radiotherapy is the treatment of choice in exophthalmic goiter. They also believe that electrotherapy is good adjuvant treatment especially in intervals of respite from radiotherapy. One of the authors' patients, having had her exophthalmic goiter cured, returned 6 years later with complete tachy-arrhythmia. This disappeared in the course of a treatment by thyroid radiotherapy. This observation showed that in a case of exophthalmic goiter with complete arrhythmia, radiotherapy may be expected to ameliorate not only the cardinal symptoms of the disease but the complete arrhythmia as well.

As other medical agents, the authors recommend iodin, sodium borate and Coulaud's serum. Radiotherapy has the disadvantage of leaving adhesions capable of embarrassing surgery later: it is, therefore, rarely to be employed in toxic adenoma. In any case, the authors would not delay recourse to surgery in cases of toxic adenoma as much as in cases of exophthalmic goiter.

To the medical prescriptions directed against hyperthyroidism, we may add those which are addressed directly to the auricular fibrillation: digitalis, rest in bed, both of which have effected the disappearance of the arrhythmia. The only remedy, however, which can be counted on to relieve the complete arrhythmia is quinidine sulphate.

Surgical treatment was undertaken by the authors in cases of complete arrhythmia due to exophthalmic goiter or toxic adenomatous goiter, only after the failure of prolonged medical treatment in exophthalmic goiter; but it was employed either at the first onset or after a brief medical treatment in toxic adenoma.

With regard to the relationship between complete arrhythmia and myxedema, the authors did not observe a single case in their series. They did, however, observe seven cases of complete arrhythmia in simple goiter. The authors are convinced that simple goiter, without undergoing Basedowian transformation, constitutes in many cases, the source of formidable cardiac attacks in the future, among which may be numbered cardiac insufficiency and complete arrhythmia, symptoms which appear especially to arise from an intoxication of thyroid origin, a thyrotoxicosis.

In cases of complete arrhythmia or cardiac insufficiency complicating goiter which clinical examination does not show to be toxic adenoma, if the usual medical treatment does not give satisfactory results, recourse must be had to enucleation of the goitrous lobe. Even if the medical prescriptions have improved the patient's condition, the authors tend strongly toward advising partial thyroidectomy anyway.

Finally, in all varieties of goiter, whatever the clinical form under which it evolves, physicians and surgeons ought to familiarize themselves with the idea of complete arrhythmia and cardiac insufficiency which are in many cases dependent upon an intoxication of thyroid origin and in which in order to prevent and cure the cardiac attacks, the thyroid lesion must be treated medically, or if need be, surgically.

Interferometric Investigations on the Question of Old Age Especially in Consuming Arteriosclerosis. — F. M. Groedel and G. Hubert. (*Deut. med. Wochenschr.*, **52** : 1981, 1926.)

According to Lorand, the final cause of premature old age is the degeneration of the various endocrine glands. Therapeutically he recommends therefore the administration of hormone extracts and iodin, the most important ingredient of the thyroid, as actual specifics against manifestations of old age. The authors themselves have observed patients with sclerosis, in whom frequently after years of good health, a sudden break-down of strength was noted among manifestations which resembled endocrine disturbances thoroughly. The disease pictures differed widely. Sometimes there were symptoms suggestive of hypofunction of the thyroid gland, and at other times, of hyperfunction of this gland. In one case, there existed lessened, in another abnormally increased sexual impulse, etc. On the whole, they had the impression that the sclerotic changes in general do not so greatly injure the vitality of the individual or endanger life energy and duration of life. Only when the changes develop with excessional speed and intensity in definite organs does there result a general break-down. This fact is very well known among other things from coronary sclerosis, sclerotic contracted kidneys, etc. The above mentioned diseases

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pictures are to be interpreted as no other than sudden aging of the entire body, owing to the deficiency of an important gland.

Since the interferometric modification of the Abderhalden reaction (as Paul Hirsch has suggested it) makes it possible to specify the disturbances of the endocrine system, the authors endeavored to solve the question with this method. They investigated for carcinoma (interferometrically) the blood from a 78 year old woman, who had been entirely healthy until the appearance of exceedingly rapid senile deterioration. The carcinoma suspicion was shown to be unfounded; on the other hand, the thyroid, ovaries and pituitary were found to be abnormally exhausted, and indeed, all three glands to an almost identical degree. From this finding, the authors infer a hypofunction of these three glands — in the aforesaid case as sequel to a senile change.

That the hypofunction of the sexual glands actually corresponds to a strongly elevated interferometric exhaustion value, the following two cases can demonstrate: A man aged 53 years, with excessive hypertonia, physically very strong, with no clinical symptoms of renal disorder. Thrice in the course of the last 2 years, he has had attacks of cerebral pseudo-embolism. Each time the symptoms receded after some hours. The patient remarked that he had never had great sexual desire, and that recently libido had been almost extinguished. Besides a high rate of decomposition for the sclerotic kidney and a still somewhat higher rate for the normal kidney — the authors infer a compensated, non-progressive renal sclerosis — the decomposition rate for the testicles surpassed by far that of all other endocrine glands. There is, therefore, obviously a dysfunction or hypofunction of the testis in this case.

The second case was that of a female patient, aged 45 years, likewise with sexual hypofunction. By interferometric investigation, the decomposition rate for the testicle was shown to be abnormally high. On the other hand, in a greatly reduced sclerotic patient (55 years), marked hystero-depressive neurasthenic characteristics were observed. The nervous symptoms suggested a beginning cerebral sclerosis. Clinically, slight dilatation of the aorta, albumin traces in the urine and hyaline cylinders were found. The interferometric investigation showed a slight decomposition rate for testicle, a strikingly increased decomposition rate for thymus and thyroid and an increase for pituitary. Here, therefore, the endocrine sclerotic disturbance is to be sought entirely outside of the sexual sphere, probably in the thyroid and thymus. The extremely high decomposition rate for arteriosclerotic kidneys is, incidentally, an important hint to revise the clinical diagnosis. In the case described, we may assume pluriglandular sclerotic disturbances, with the exception of the testis.

The authors describe a still greater number of cases, among which some showed considerably increased decomposition rate for the testis, besides increased decomposition rate for other glands, consequently, pluriglandular changes of senile nature. In any case, if we desire to draw conclusions from the interferometric observations in consuming arteriosclerosis, we can call especial attention to two factors as fairly well demonstrated:

(1) In consuming arteriosclerosis very frequently a marked cellular deterioration of the endocrine organs may be determined, and with it the hypofunction of the involved glands.

(2) All glands can be attacked by this senile decomposition, in some cases only one gland or one gland predominately, in other cases several glands at the same time.

A Case of Melancholia Associated with Vitiligo. — C. J. Parhon and M. Désévici. (*Bull. mém. Soc. méd. hôp. Paris*, **43** : 39, Jan. 27, 1927.)

Recently the authors had the opportunity to observe a patient presenting melancholia simultaneously with patches of vitiligo and leucotrichia. The patient was a woman, 35 years of age, who entered the hospital owing to psychic disturbances of depressive character. The authors question whether there is a relationship between the psychic syndrome and the cutaneous dystrophy. Syphilis has often been incriminated in the etiology of vitiligo but no symptoms of syphilis could be observed in the present case; laboratory analysis and the patient's history were also negative in this respect. The authors then turned their attention to disorders of the endocrine functions.

Vitiligo has several times been seen in association with exophthalmic goiter. Thyroid disorder is, in fact, able to give an explanation for the depigmentation of the hair and Sainton and Peynet have looked upon vitiligo as a prolongation of leucotrichia.

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One of the authors (Parhon), in collaboration with Savini, has already directed attention to the depigmentation of feathers under the influence of thyroid treatment, and the vitiligo of Basedowians, as well.

The patient in the authors' case is not an exophthalmic goiter case; but she may be considered as hyperthyroid: the slight tachycardia, the brilliancy of her eyes, the enlargement of the thyroid gland, pulsations of the carotids, crises of diarrhea, suggest this.

Researches of Laignel-Lavastine as well as those of one of the authors have shown the importance of the thyroid factor in melancholia. In conclusion, the authors believe that the presence of vitiligo and melancholia in their case is not a simple coincidence. The two disorders can be explained by a common pathogenetic factor represented by exaggeration of the thyroid function and perhaps also by a certain degree of dysthyroidism.

Suprarenal Insufficiency and Diphtheria. — Lereboullet. (*Presse méd.*, 35 : 137, Jan. 29, 1927.)

The author reports a series of observations which led him to admit the rôle of adrenal insufficiency in severe diphtheria. Experimentation has for some time past brought to light the importance of capsular alterations in experimental toxic diphtheria. Pathologic anatomy shows, in human diphtheria, a high proportion of evident capsular lesions: in one case in five at least, capsular hemorrhages have been found in children who succumbed to malignant diphtheria.

Clinically, the author has joined with Hutinel, Martin and Darré in stressing the significance of observed signs, outside of the secondary malignant syndrome of diphtheria, and raised the hypothesis of adrenal insufficiency at their origin. Since 1922, he (with P.-L. Marie and Leprat, and recently with M. Pierrot) has systematically investigated the hypoglycemia in severe diphtheria. He met with it frequently, and in the 30 cases studied with M. Pierrot, the great majority had a distinctly lowered glycemia, varying from 0.45 to 0.80, which returned to normal with convalescence. This hypoglycemia, which resembles that of Addisonians, seems to form a biologic argument to be joined to the preceding ones in favor of the rôle of adrenal insufficiency in diphtheria.

This idea has an important practical significance. Systematic adrenal organotherapy permits of better treatment and better chance of recovery in severe cases of diphtheria. Lereboullet has been able to reduce to less than 20 per cent the mortality from malignant diphtheria in his service, and he owes this not only to massive serotherapy but to adrenal organotherapy as well. The latter, given subcutaneously and by mouth at the same time, gave him very encouraging results. They are, however, a valuable measure in malignant diphtheria. If the effects of adrenal organotherapy can be regarded as purely symptomatic, owing to its evident cardiovascular action, we must recognize this one cord of therapeutic action with the other observations and conclude upon the importance of the rôle of suprarenal alterations in the production of accidents observed in the course of malignant diphtherias.

M. Lesné, in his service at the Trousseau hospital, observes, as does M. Lereboullet, the frequency of suprarenal insufficiency in diphtheria, and like him, he uses adrenalin but in applying it on the nasal and buccal mucosae and in small doses, owing to the sudden shock which it at times occasions. Various symptoms (enlarged liver, tachycardia, etc.) can not, however, be explained by suprarenal insufficiency. Bulbar intoxication is one of the causes of death. Along with suprarenal treatment, he recommends recourse to large doses of serum and to adjuvant remedies.

The Causes of Chronic Constipation. — H. Steindl. (*Wien. klin. Wochenschr.*, 39 : 1457, 1926.)

In the course of descriptions of the various causes of spastic constipation, the author draws attention also to those forms of constipation which may be traced back to disturbances of the endocrine glands or which form a constant accompanying symptom of definite diseases of the endocrine glands. The author, for example, mentions the obstinate constipation in myxedema, the retention of feces in positive disease forms, associated with sex gland disturbances (infantilism) etc. The type of constipation which one encounters in a group of relatively underdeveloped girls is well known (genital hypoplasia, chlorosis, etc.), of which disturbances of the glands of internal secretion surely are the underlying cause. We may recall the group of young female individuals (16 to 20 years), constantly to be observed, with their

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boundless complex of symptoms, who consult the physician or are brought to him chiefly because of their poor appearance, and a thorough examination of whom (to which Schur also alludes recently in another connection) could determine: chronic, often painful digestive complaints, loss of appetite, most obstinate constipation, headaches, slight rise in temperature, menstrual disturbances, with entirely normal heart and lung findings. The blood findings suggest anemia or chlorosis. Frequently, outside of the existing signs of degeneration, these girls also show hypoplasia of the genitalia, functional weakness, symptoms of the vegetative system (sympathico-vagotonia, etc.).

The constipation appearing in this symptom complex results in symptoms of stoppage and accumulation of feces, pains in the appendix and in the region of the cecum, cecal splashing, sensitiveness to pressure in this region, which when associated with rise in temperature in these patients can easily lead to an incorrect diagnosis of appendicitis and to an incorrectly undertaken operative intervention. In fact, such patients are subjected to appendectomy to no purpose (at times, owing to the false interpretation of symptoms, they are submitted to gall-bladder or stomach operations). After these operations the persistence of the old complaints reveals the false scent of the diagnosis and of the undertaken therapy.

Functional changes in the vegetative nervous system (weakness, conditions of stimulation, and others), which may be attributable to disease of the endocrine glands, lie presumably at the basis of all of these forms of constipation symptoms mentioned.

Advances in Ovarian Hormone Research through a New Specific Test Object. — Fels. (*Klin. Wochenschr.*, **5** : 1729, 1926.)

Recapitulation of the previous investigations in which in particular Allen and Doisy, as well as Zondek and Aschheim have a share. The investigations of the author were concerned with the demonstration of the ovarian hormone in the blood through calling forth the estrous cycle in the castrated mouse. This problem has up to the present been treated only by Loewe. Loewe's method for cell counting on the streak of the vaginal secretion is challenged. In general, work was carried on with 2 cc. serum, since it was shown that when 2 cc. were inactive, 3 and 4 also remained so; on the other hand, when these amounts were active, often a not quite clear reaction appeared with less. The result of the injection was always negative in the non-pregnant. The same result was given by liquor amnii, ovarian cystic fluid and human milk. Concerning cerebrospinal fluid nothing can as yet be said; the result in the first 3 months of pregnancy was likewise negative. In the third to the sixth months, the results were changeable and tended clearly toward the positive as time went on. From the sixth month of pregnancy, estrus was excited in all experiments with the serum. Likewise, retroplacental and umbilical cord blood was positive.

Six hours after delivery the reaction was still present; later, it was no longer present. A conclusion *a posteriori* on the content of hormonal substance of the blood from the transient prolongation of the estrous cycle was rejected since normally estrus admits of great variations.

From the results, it follows that in human beings in the later months of pregnancy, a marked increase of hormonal substances appears in the blood, in which then also the umbilical cord blood takes part. This fact can perhaps serve as support for the view that the placenta is not only the depot but also the site of formation of the hormone, since the other sites of formation, such as corpus luteum of pregnancy and ovarian cortex are only effective in the earlier months of pregnancy in the experiment; so that for the hormone increase in late pregnancy just the placenta still remains left over. Furthermore, the evidence for an hypothesis is brought with it, as it was advanced in the addition to the works of Halban. Through these works we know that in the later months of pregnancy on the one hand the fetal female generative organs grow exceedingly more rapidly, whereas the male organs experience a retrogressive movement. The hormone of the ovary and placenta has been made responsible for it, — the investigations of the author justify this view.

On the Use of Concentrated Solutions of Insulin. — P. Mahler. (*Deut. med. Wochenschr.*, **52** : 1172, 1926.)

Wiechowski, the head of the Pharmacological Institute of the German University at Prague, had produced insulin in concentrated form as early as the year 1923 from various

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elements and indeed of such a strength that 1 cc. contained 100 or 150 units. The patients learned how to compute everything in the shortest possible time and many of them understood it even surprisingly well, so that they were able to calculate exactly the necessary amount of insulin suitable to the different forms of diet. All, however, asserted unanimously that this form of injection was much more agreeable and caused almost no pain. It could be observed objectively that patients who had a poor tolerance for the different brands of insulin, showed neither redness nor swelling as soon as the concentrated preparation was made use of. The only misgiving, the fear of hypoglycemia, falls away of itself, according to the generally confirmed experiences, provided that the physician abides by the decision to deliver insulin only into the hands of well educated patients who understand the dosage of their preparation.

A Case of Diabetes Mellitus in a Child, Treatment of Which with Insulin Influenced Growth Favorably. — Chabanier, Lebert and Lumière. (*Paris méd.*, **16** : 603, 1926.)

The authors report a case of juvenile diabetes mellitus in which growth which had come to a standstill with the appearance of the disease, again took its normal course under the influence of insulin. The case was that of a 12 year old child, in whom diabetes appeared quite suddenly and brought the hitherto normal growth to a standstill, occasioned a marked sudden fall in weight, with deterioration of the general condition. Insulin rapidly cleared away the glycosuria and acetonuria, which have now remained absent for 2 months. At the same time, the general condition improved, weight increased (in 10 months) about 6 kg., and growth again resumed its course.

Such a result is, however, not always to be ascribed to insulin.

Concerning the Use of Intravenous Pituitary Sodium Chloride Infusion in the Treatment of Poisoning with Oleum Chenopodii. — Vogt. (*Klin. Wochenschr.*, **5** : 1638, 1926.)

Severe symptoms of poisoning appeared in a woman who had exceeded the maximum dose of about 12 drops of Oleum Chenopodii. Lavage of the stomach with ricinus oil and the injection of heart remedies did not impro her condition. A high intestinal enema w also without effect, as well as the injecti of pituitary. In this critical condition, t author made an experiment with the int venous infusion of pituitary sodium chlori which he had used for a long time past wi advantage in the control of post-operati intestinal paralysis. As a matter of fac he succeeded through the application of 6 gm. physiological NaCl solution and ampoules of pituitrin in bringing about thorough evacuation in the shortest possibl time. The author recommends this medica tion not only in intoxications with Oleum Chenopodii, but also quite generally in the therapy of other poisonings in which evacua tion of the intestine must be striven for as wnere no other contraindication is present.

A Human Ovum Approximately Nineteen Days Old. — J. P. Greenhill. (*Surg. Gynecol. and Obstet.*, **44** : 493, Oct., 1927.)

Exactly fifty human ova less than 3 weeks old have been described more or less thoroughly during the last five decades. It has been the custom of nearly all authors who have reported young human ova to give the age of their ova in days. Most authors have stated the age with great assuredness. Such positive assertions should not be made, however, because there is no accurate criteria for determining the age of early ova. Many important factors concerned in human reproduction are as yet not fully understood.

Greenhill describes a young human ovum obtained in an aborted decidual cast and gives the measurements. The outstanding feature of this ovum is the unusual amount of invasion of the decidua by plasmodium. There very abundant trophoblast, especially plas moditrophoblast, in the intervillous spaces. There are numerous definitive villi, some of which have begun to branch. Blood vessel anlagen are found in the mesoderm of the chorionic vesicle, the villi, the body stalk and the yolk sac. The few preserved sections of the embryo show a small amniotic vesicle and an embryonic shield lying upon a large yolk sac. In the decidua capsularis is an operculum deciduae which appears to consist of fetal ectoderm and is attached to the chorion laeve by a strand of plasmodium. The decidual reaction is more pronounced in the stroma cells than in the glands. Some of the large veins in the spongiosa beneath

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ovum communicate with the intervillous space and contain free masses of plasmodium. The development of this ovum tallies with ova considered to have a maximum age of 19 days.

Hypotensive Effects of Insulin. Letter from Paris Correspondent. — (*J. Am. Med. Assn.*, **92** : 573, Feb. 16, 1929.)

P. Gley and Kisthinios, in a report, showed that insulin lowers the blood pressure and that this hypotension is not due to the substance that diminishes the blood sugar but to a distinct hypotensive substance.

In a second report Kisthinios gave the results of insulin treatment in several cases of hypertension. In all the patients the decrease in pressure was accompanied by improvement in their subjective and functional disturbances.

In a third report by R. Giroux and Kisthinios were the results of an investigation of the effects of insulin on angina pectoris in non-diabetic patients. They reported four cases in which this treatment stopped the attacks for several months and brought about a diminution in the opacity of the aorta as shown by roentgenograms.

Utilization of the Calcium of Spinach. —Laura McLaughlin. (*J. Biol. Chem.*, **74** : 455, Sept., 1927.)

Spinach, fed for 6 days as the only food high in calcium in a diet consisting of some of the most commonly used foods produced distinctly positive calcium balances in six out of seven healthy women and calcium equilibrium in the seventh. Spinach furnished 70 per cent of the calcium, and the intake was greater than the calculated requirement for maintenance. It was thought that the repeated use of an unusually large quantity of spinach would emphasize any tendency toward hindrance to calcium assimilation through presence of fiber or oxalates, but no such tendency was demonstrated. Storage of calcium in adult women is assumed to demonstrate a utilization of the calcium of spinach.

Diabetes Mellitus and Concomitant Leukemia. — Jerome Glaser. (*J. Am. Med. Assn.*, **88** : 1626, May 21, 1927.)

The simultaneous occurrence of diabetes mellitus and leukemia in the same person is so unusual that Glaser reports this case. Of four other cases previously reported in the literature three came to necropsy, and in none of these did microscopic examination of the pancreas reveal evidence of leukemic infiltration. Therefore, the simultaneous occurrence of diabetes mellitus and leukemia in these cases, at least, can not be explained on the basis of leukemic infiltration of the pancreas.

In the author's case here described, the pathologic evidence of myelogenous leukemia in the spleen and retroperitoneal lymph nodes, together with the qualitative changes in the blood picture without any marked increase in the total leukocyte count, classified the condition as myelogenous leukemia of the aleukemic type. Another unusual feature of the case was the pigmentation of the skin. Bronzing similar in appearance to this occurs in the so-called bronze diabetes, in which group the pathologic observations showed this case not to belong. Such bronzing does not occur in diabetes mellitus.

An explanation of the unusual pigmentation which occurred in the author's case may be found in the theories of Féréol and Nieskowski and of Paget and Fowler. They believed that pigmentation associated with lymphadenopathy is due to disturbance of the sympathetic nervous system and through this of the suprarenals, by pressure of enlarged abdominal lymph nodes on the abdominal sympathetic chains and ganglions. Another and later theory is that of Peters, who made the suggestion based on work by Eppinger, that an injured liver may be unable to perform its normal function of removing melanin from the circulation and may permit an excess of it to reach other body tissues, thus giving rise to excessive pigmentation.

Blood-Sugar Estimations in the Treatment of Diabetic Coma. — Philip Bayer and A. Victor Neale. (*Lancet*, **216** : 129, Jan. 19, 1929.)

Diabetes mellitus sometimes presents unusual features in childhood. The authors observed a diabetic child who had a blood-sugar of about 40 mg. per cent over a period of a few weeks without any adverse signs or symptoms. They believe that this may not be very unusual in children. They report a case illustrating this and the difficulty it causes in the treatment.

A girl, aged 13 years, was admitted to hospital in a state of semi-coma. The urine contained 6 per cent sugar. She was treated with

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140 units of insulin (in 20-unit doses), and as the urine still contained 1.8 per cent of sugar a further 10 units of insulin were given.

During the period it was not possible to obtain blood-sugar estimations, but 1 hour after the last dose of insulin the blood-sugar was 13 mg. per cent. Clinically the child had passed from hyper- to hypo-glycemia, but still retained the glycosuria.

It was manifest that the renal threshold had been completely disorganized and, for the time being, the kidneys were allowing sugar to escape despite a subnormal blood-sugar. This rendered it essential that further treatment should be controlled by frequent blood-sugar estimations.

After the state of coma had been overcome a great susceptibility to insulin occurred, the blood-sugar being reduced from 283 mg. per cent to 115 mg. per cent with 10 units of insulin, the urinary sugar falling from 3.8 per cent to 2.0 per cent at the same time. This further illustrated the value of blood-sugar estimations.

Large doses of glucose were required to raise the blood-sugar to normal limits, apparently because of the extreme degree of renal leakage and prolonged effect of insulin.

Four weeks after admission the renal threshold for glucose had improved, but had not become normal. A recent re-examination shows the persistence of the abnormal renal threshold.

Cases of Diabetes Mellitus with a Low Renal Threshold. — R. D. Lawrence. (*Brit. Med. J.*, **3552** : 196, Feb. 2, 1929.)

There seems no reason to think that the combination of diabetes mellitus with a lowered renal threshold is not a mere coincidence.

Hjärne has recently published a hereditary study of renal glycosuria which tends to show the absence of any connection between diabetes mellitus and renal glycosuria.

The most likely explanation of these cases is the fortuitous development of true diabetes in cases of renal glycosuria. It is well known that a lowered threshold is fairly common in normal individuals.

These cases seem, on the whole, to follow the same course as diabetes with a normal renal threshold. These cases respond to treatment, apparently, in the usual way but present some difficulty in their management.

It is difficult to see any etiological connection between the lowered threshold and diabetes in these cases. It is highly improbable that the diabetes produces in some way a lowering of the threshold, for any change that is known to take place in diabetes is in the direction of a rise in the threshold.

Mumps Orchitis with Especial Reference to Sterility. — Francis Patton Thenem. (*New England J. Med.*, 199 : 12… Dec. 20, 1928.)

With occasional exceptions, orchitis in mumps is confined to the period of puberty and adolescence. In the majority of cases the orchitis is unilateral, and for some unknown reason, the right testicle is more frequently involved than the left. Wesselhoeft found, from a study of the literature, that out of 1208 cases of orchitis, 209 cases were bilateral. It may be said that out of all cases of mumps about 1 out of 6 has orchitis and that of these orchitic cases about 1 of 6 is bilateral orchitis. In other words, approximately 3 per cent of all cases of mumps develop a bilateral orchitis and hence are in some danger of subsequent sterility. In these cases of bilateral orchitis, there frequently follows a greater or less degree of testicular atrophy.

Opinions differ as to what may be done to prevent the development of orchitis in beginning cases of mumps. Fougerousse states that it was shown at the U. S. Naval Hospital at New Orleans that the early treatment of mumps with convalescent serum is an efficient preventive of orchitis. Cheinisse believes that convalescent serum in mumps is not specific and that certain experiments indicate that normal serum would be just as effective. The author says that in cases of incipient mumps the use of mumps convalescent serum with a view to lessening the severity of the disease and of avoiding orchitis is well worth a trial.

Sterility due to orchitis is often present without any loss of sexual desire or potency and without any abnormality of secondary sex characters. Investigators who favor the use of diphtheria antitoxin and those who favor the use of convalescent mumps serum as means of preventing the development of orchitis, believe that these means, if employed early in orchitis, will help to prevent subsequent testicular atrophy. The author believes that the work done thus far has been insufficient to establish the truth of the matter conclusively. He says that probably the most promising method known at present to …

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vent or lessen testicular atrophy is surgical. He adds that the testes are not the only genital organs that may be affected in mumps. Destruction of the epididymis and vas deferens, and atrophy of the prostate and Cowper's glands may also occur.

Sulphur as a Remedy for Diabetes. — Contribution of the Discoverer, Prof. Bürgi. (*Neue Freie Presse*, **22363** : 3, Dec. 17, 1926.)

The discoverer of the new remedy for diabetes, Prof. Emil Bürgi, who in association with Dr. Gordonow made the discovery that sulphur is capable of lowering the sugar content of the blood, reports the following:

About 2 years ago, Prof. Bürgi began to concern himself with the question of how sulphur acts on the metabolism. Sulphur is a substance which has for a long time been prized as a remedy for everything possible and for this very reason has fallen into discredit. For several years past, interest has grown especially because there have been observed definite results in chronic articular rheumatism, bone tuberculosis and skin diseases from sulphur baths. In order to discover the fundamental action, the author investigated the metabolism of animals. He then, in association with Dr. Gordonow and Prof. Wegerlin, determined that in animals which receive sulphur, glycogen increases in the liver, whereas the content of the blood in sugar becomes less and the basal deposit sinks. This all stands in a causal relationship. Since in diabetes, the reverse is the case, *i. e.*, the liver breaks up glycogen which is nothing other than animal starch, too quickly, and sends too much sugar into the blood, this action of sulphur can certainly be employed in diabetes.

The testimony of Abel and Geiling concerning insulin is in part concordant with these experiments, which since that time have been corroborated by other workers. Insulin is a so-called internal secretion, that is secreted by the pancreas and hinders glycogen decomposition in the liver and principally for this reason represents the best remedy for diabetes at the present time. Since it can, however, occasion dangerous secondary phenomena, the milder treatment with sulphur would perhaps be preferable.

The author represents the action as mild and not energetic, so that in general a longer course of treatment should be given. Insulin is not a remedy which definitely cures diabetes, but merely removes the severe symptoms for a time. Insulin has a stronger action than sulphur, but it is possible to give sulphur to patients for months, even years, which can not be the case with insulin. The chemical experiences concerning the actions of sulphur in diabetes are of course not yet sufficient, although on the whole they speak in favor of the correctness of Bürgi's experiment.

Sudden Death in an Eczematous Child with Hypertrophied Thymus. — Houcke and Martin. (*Presse méd.*, 35:57, Jan. 12, 1927.)

Report of a case of sudden death in the course of an attack of dyspnea in a child of 20 months, very healthy in appearance, but with weeping eczema of the scalp. Autopsy revealed a thymic hypertrophy without compression of the neighboring organs. The thymus weighed 23 gm. and histological examination confirmed the preceding data.

In this case, it seems that the eczema and sudden death may be related to a dysfunction of the thymus. There would, therefore, be a primary interest in keeping a lookout for thymic hypertrophy in eczematous infants, by means of radiography, in order to treat this lesion with radiotherapy or even with surgery.

Specific Dynamic Effect. Pituitary Anterior Lobe and Obesity. — O. Kestner, R. Liebeschütz and H. Schadow. (*Klin. Wochenschr.*, **5** : 1646, 1926.)

The authors could determine that human beings with increased fat deposit had a too low specific dynamic action. Through the administration of anterior lobe of the pituitary, the specific dynamic action could be raised. With pituitary anterior lobe they were able to reduce the corpulency of healthy and diseased individuals, even if but slowly. The lowering of basal metabolism with pituitary anterior lobe, already observed by Liebesny is opposed to this idea, however. If a reducing effect is therefore actually desired, thyroxin and pituitary anterior lobe should be combined. With the combination of pituitary anterior lobe and 0.1 up to 0.2 glandula thyroidea, the authors never observed any complaints whatever in the course of treatment of many months. Still, they hold it correct not to combine the remedy in one preparation, but to give the extracts separately, so that the physician can adjust the treatment.

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Are Insulin and Hydrocyanic Acid Antidotes? — Szolnoki. (*Deut. med. Wochenschr.*, **52** : 1427, 1926.)

In animal experiments, the action of cyanide was inhibited by insulin; after 24 hours a dose of insulin could restore oxidation in severe cyanide symptoms. In any case, it is a task for further investigation to determine the antagonism between insulin and cyanide of potassium.

Until now, those poisoned severely by cyanide were irretrievably lost. Insulin as oxidation promoter was not applied in human beings in similar cases. With a certain plausibility the intravenous injection of insulin can be tried in cyanide of potassium poisoning as the last resort, just as in coma, in large doses (30 units and more) with simultaneous administration of grape sugar.

Suprarenal Migraine Successfully Treated by Organotherapy. — Jacques-Sébillot. (*Progrès méd.*, **3** : 107, Jan. 15, 1927.)

For the second time, the author presented the case of a patient completely cured for the past year by suprarenal organotherapy of very frequent, violent and refractory attacks of migraine of suprarenal origin (five a month). Organotherapy has been discontinued for the past 3 months and the patient has continued on an ensemble of "kinesitherapeutic methods of endocrine stimulation." The whole treatment has given not only cure of the headaches but an actual restoration of physical and moral health, as well.

Treatment of Diabetes with Insulin and Diet. — H. W. Jansen and P. Müller. (*Münch. med. Wochenschr.*, **73** : 1687, 1926.)

Description of the practical application of insulin. With the dietetic-insulin treatment for the purpose of raising the tolerance, the authors obtained a higher tolerance for carbohydrate and calories in the majority of cases than was usually seen in the purely dietetic treatment. With this improvement in tolerance, there was also associated a rise in the general state of health and — especially in patients in a condition of undernutrition — a gain in weight and improvement in strength. A peculiar, not to be underestimated advantage of dietetic-insulin therapy needs to be mentioned: The ketonuria sometimes present at the outset and appearing especially with the institution of diet with restriction of carbohydrate, which can develop in a particularly threatening manner, disappears at once or after several days with insulin treatment. Besides, it was at times shown that the urinary sugar had already disappeared while the urinary acetone still remained present for several days. The origin of this acetone is not clear. In every case this ketonuria had no practical significance and soon disappeared again.

The authors had favorable experiences with insulin-dietetic therapy in the treatment of tuberculous infections, complicated by diabetes. Of course, this therapy permits of a richer nutrition than through simple dietetic treatment and makes possible an improvement of the state of nutrition and with it an increase in strength, which is of decisive influence for the course of tuberculosis. For the treatment of diabetics with tuberculous complications, higher doses of insulin are frequently required, in order to obviate an exacerbation of the extremely dangerous state of metabolism through the infection.

Treatment of Nephrosis with Thyroidin Tablets (Richter). — L. Jehle. (*Wien. med. Wochenschr.*, **76** : 167, 1926.)

The author refers to Eppinger's communications on the efficacy of thyroid preparations in edema of patients suffering from nephrosis and reports that the cure effected by thyroid treatment, so far as his observations are concerned, may persist for 1½ years without recurrence. Thyroidin increases diuresis, eliminates dropsy and brings about the extraordinarily rapid retrogression of albuminuria in cases with a high amount of albumin contained in the urine.

In one case the author had the impression that the child was draining his hydrothorax. Also, the high recumbent position of the legs was accompanied by striking result in one case (60 per cent albumin).

The author is of the opinion that nephritis and nephrosis are systemic diseases occasioned by the establishment of a circulus vitiosus. Thyroidin treatment breaks this cycle owing to its favorable influence on the tissue.

In another series of observations, the author obtained good results and important increases in weight through the long continued administration of thyroidin (3 to 4 tablets per day) and elevation of the legs, in orthostatic albuminuria.

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On the Objectivation of Sex Gland Function. — Anton Lieben. (*Wien. klin. Wochenschr.*, **39** : 1159, 1926.)

Functional disturbances of the sex glands in the male are conditioned either by a primary disease of the organ or secondarily through disturbance of the hormone equilibrium. With regard to the latter type of sex gland insufficiency, we know that disease of almost every endocrine gland is capable of causing damage to the sex glands; that impotence appears in exophthalmic goiter as well as in myxedema, and in pancreatic diabetes. The influence of the pituitary on the sex glands is also evident.

The treatment of impotence offers the physician especial difficulties when the influences of the endocrine glands are not perceptible forthwith. Indeed, Liebesny was the first to demonstrate that it was possible by investigation of energy metabolism to analyse the existing hormone conditions in sex gland disturbances, and according to the declaration of this author, the basal metabolism (consumption of oxygen in resting, fasting condition) as well as the specific dynamic effect of nutrition (increase in consumption of oxygen following supply of food within a definite experimental time) must be investigated in similar disturbances. A decrease in basal metabolism was found in cases with primary sex gland insufficiency. Since this lowering of basal metabolism is, however, also found in primary hypofunction of the thyroid gland, it is necessary to be able to determine by still another method whether the sex gland hypofunction is primary. Liebesny has indeed shown that in cases of primary sex gland hypofunction, low basal metabolism, but often relatively high value for the specific dynamic effect, exists. This rise in specific dynamic action is probably to be related to the pituitary, which arises from the fact that numerous authors were able to determine in animals and in man an essential increase in the size of the pituitary. At all events, the method of Liebesny, in the critical examination of a hormonal genesis, is able to give valuable enlightenment on sex gland disturbance. Hence, before introducing a treatment for impotence, investigations of the energy metabolism must be carried out, since in this way we are enabled (of course, with close consideration of the symptomatology) to obtain important objective hints for the hormonal genesis of a sex gland functional disturbance.

Menorrhagia with an Apparently Normal Pelvis. — J. L. T. Isbister. (*Med. J. Australia*, **2** : 165, Aug. 11, 1928.)

Excessive uterine bleeding often has a constitutional and not a local origin. The real cause is easily overlooked in many cases. Pernicious anemia in the early stages may cause menorrhagia though as a rule the disease is associated with amenorrhea. Osler mentions a form arising after pregnancy and also the occurrence of hemorrhage with this and also in aplastic anemia which so often arises in young women. In myxedema a good deal of confusion has arisen, but it is certain that menorrhagia does occur. The impression that amenorrhea is common has arisen because 44 per cent of the patients are past the climacteric, when the myxedema develops. The possibility of thyroid deficiency should always be thought of in diagnosis. Bell says that exophthalmic goiter, in the very early stages, may give rise to menorrhagia and in the later stages to amenorrhea. There is a menorrhagia with an enlarged thyroid which occurs in girls at puberty and can be controlled by calcium lactate. Sehrt reports that of 85 patients with functional menorrhagia without any pelvic lesions 69 per cent suffered from hypothyroidism. Mitral stenosis is sometimes associated with menorrhagia. Masturbation and sexual excess may cause menorrhagia. Another cause is superlactation. The treatment here is to wean the child and give good doses of calcium lactate. The author adds that during the malignant influenza epidemic of 1919 a very large percentage of women suffered from menorrhagia.

Shaw has shown that with inflammatory conditions in and around the ovaries the cyclical functions of the ovary are not inhibited, but on the contrary menorrhagia is common. Histologically there is increase of lutein tissue in the corpora lutea and this leads to increased menstruation. No less than 38 per cent of patients with pelvic infection suffer from menorrhagia. The peritonitis may come from the appendix as well as the tubes; if from the upper or peritoneal aspect it is less likely to cause menorrhagia, than if it came from below, because when from below, the uterus itself will be infected and be more likely to bleed. And so the ovaries, fixed and matted with adhesions,

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often cause menorrhagia. Very slight pathological changes in the ovary may produce most severe menstrual changes. The corpus luteum plays the part of an organ of internal secretion and influences the thyroid and pituitary. Many of the cases of functional hemorrhage so-called, no doubt, fall under the heading of menorrhagia due to unrecognized constitutional causes and some also are due to ovarian pathological causes. Idiopathic or essential or functional menorrhagia, is commonest at puberty or the menopause. While there is no obvious pathological cause, yet there must of necessity be some pathological state causing it.

Whitehouse has demonstrated that with the functional or essential menorrhagia of puberty and the menopause there is hyperplasia and consequent overaction of the ovary, causing a too frequent period. Consequently curettage often does no good because it can not alter the ovarian condition. Some good may be done by inhibiting not the ovary, but the accessory sex glands, the thyroid or the pituitary. X-rays applied to the thyroid may be beneficial and Whitehouse has been using injections of extracts of corpus luteum. One should not be in too great a hurry to cure such patients. It takes time for the various sex glands at puberty to settle down and accommodate themselves to each other and work steadily and in harmony. In a second class patients suffer from periods that are not too frequent but too long and also without clots like the former class. These are now thought to be due to over-activity of the ovary producing too much hormone and making the uterus bleed. Whitehouse says such patients are benefited by curettage and frequently cured. The reason is not quite understood. Novak urges the importance of diagnostic curettage. In many cases it affords a permanent cure and he advised recurettage as the best treatment for young women. There is another class of patients, usually older, who suffer from severe hemorrhage due to an intrinsic uterine cause. Diagnostic curettage in these cases is most important.

Of late years x-rays and radium have been used successfully in many cases of intractable menorrhagia. Many authorities think it is attended with some risk in the young and child-bearing age. Organotherapy, with the exception of thyroid and pituitary have not proved satisfactory according to the author. Corpus luteum, orally, Novak says, is unsatisfactory. Whitehouse uses an injection of corpora lutea.

Menstruation and Working Capacity. — Letter from London Correspondent. (*Am. Med. Assn.*, **90** : 1882, June 9, 1928.)

The Industrial Fatigue Research Board has concluded, after an important research into the effects of menstruation on working capacity, that menstruation as a rule has no noticeable effect on the working capacity of healthy women.

Raynaud's Disease Successfully Treated with Insulin. — L. Blum and A. Weil. (*Presse méd.*, **35** : 89, Jan. 19, 1927.)

A patient, 39 years old, with Raynaud's disease, to whom rest, heat and sedatives brought no relief, was given insulin treatment. At the end of 10 days, there was distinct improvement, which soon changed to a true clinical recovery.

Practical Therapeutics

(*Continued from page 81*)

Finally thyroid therapy performs great service in goiter treatment. It works with iodin in these cases, yet has the advantage over iodin in that it causes the disappearance simultaneously of hypothyroid phenomena frequently appearing in goiter. The presence of exophthalmic goiter symptoms alone represents a contraindication. Outside of the latter, the following contraindications to thyroid therapy are also to be mentioned. Marked lability of the vegetative nervous system, non-compensating defect of cardiac valves, angina pectoris, tuberculosis, chronic nephritis and severe diabetes.

Of great importance is the dosage. In myxedema relatively high doses can be given, 0.2 to 0.3 gm. desiccated thyroid gland daily. In the milder grades of hypothyroidism one half as strong a dose daily (0.1 to 0.15 gm. desiccated thyroid), or the first dose given every 2 days is sufficient. In cases, where the outbreak of hyperthyroid symptoms is to be feared it is advisable to administer more than 0.1 to 0.15 gm. desiccated thyroid extract every 2 days. The thyroid medication must as a rule be used for a long period of time.

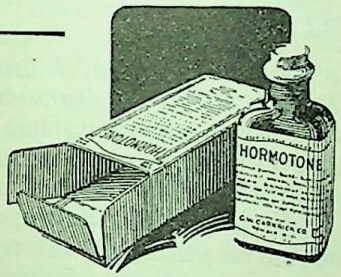
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Pituitary Infantilism with Adiposo-genital Syndrome Due to Tumor of Rathke's Pouch. — G. Guillain and J. Decourt. (*Presse med.*, **37:** 870, July 3, 1929.)

The authors present a patient of 17 years in whom a syndrome of intracranial hypertension developed at the age of 12 years with progressive lowering of vision ending in complete blindness. When the patient was brought to *La Salpêtrière*, a complete optic atrophy was noted, a midriasis with pupillary inertia and an amaurotic nystagmus. This young man presented a typical adiposogenital syndrome with infantilism and feminism; his height is 1 m. 37; the adiposity is diffuse but especially marked at the root of the extremities, in the mammary regions and on the abdomen and pubic regions; the secondary sexual characteristics are absent; the genital organs are not developed. The psychic state is that of a child of 12 years. Basal metabolism is decreased to 0.49 per cent. There is no polyuria; cerebrospinal fluid is under great tension. Radiography shows a noticeable increase in width and depth of the sella turcica with resorption of the posterior clinoid apophyses; moreover, small intra- and sub-sellar spots characteristic of tumors of Rathke's pouch are observed.

Tumors of the craneopharyngeal pouch are amenable in a number of cases to a surgical intervention by transfrontal route, for radiotherapy which is successful in pituitary adenomas is without action on these tumors. This patient would have been advised to undergo an operation if he had not come to *La Salpêtrière* completely blind. This definite loss of vision appeared a sufficient reason for not considering a serious operation the results of which could not be useful.



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The Female Sex Hormone. A Survey. — E. Poulsson. (*Norsk. Mag. Laegevidenskapen*, **90** : 175, 1929.)

The estrous reaction is not quite reliable. Animals are observed — although a positive cause can not be given — which either remain refractory, or some which first show the typical reaction with higher than the usual doses. The reaction is not limited to the vaginal changes; rather it is the uterus which is stimulated to marked growth; its weight attains an amount many times the original and likewise the mammae show not merely enlargement but secretion of milk also. Simultaneous with the genital changes an intense influence on the respiratory metabolism is observable. The "antimasculine" action is very remarkable. In young cocks following 6 weeks of treatment with the female sex hormone there is visible a distinct retrogression of the testis, of the membrum and of the seminal vesicles in comparison with the organs of untreated animals of the same age. The hormone is not species specific. With regard to the chemical properties of the hormone no certainty could be arrived at as yet. For the time being no positive statements are to be made concerning the therapeutic use of the female sex hormone either. Among the cases which seem suitable for treatment with the genital or pituitary hormone may be mentioned: conditions of hypofunction, delayed puberty, infantilism, virilism, premature climacteric. Dementia praecox, in which as a rule there exists an ovarian insufficiency, is also mentioned among the indications. Certain forms of amenorrhea are to be regarded as contraindications, which, as in tuberculosis, diabetes and nutritional diseases, are to be considered as an aid to nature. The valuable raw material for the preparation of the sexual hormone is the urine of pregnant women which also has the great technical advantage that it is free from albumin. Loewe's demonstration of the presence of estrus-inducing substance in the vegetable kingdom is very interesting.

Diabetic Polyneuritis; Remarks on the Action of Testicular Extract. — L. Cornil and Kissel. (*Presse med.*, **37** : 918, July 13, 1929.)

The authors present a patient affected with diabetic polyneuritis in whom improvement of the diabetes was begun by injections of spermatogenetic extract in the face of failure of insulin therapy. Moreover, in the course of the treatment the abolished tendino reflexes reappeared and the pain was considerably attenuated. They again draw attention to the favorable action of spermatogenetic extract in certain cases of diabetes and refer the earlier works which one of them published on this question with Jochum.

Preparation of a Substance Lowering the Calcium Content and of a Substance Lowering the Phosphate Content of the Serum. — A. Nitschke. (*Zeitschr. ges. exp. Med.*, **65** : 651, 1929.)

The author succeeded in isolating two substances from spleen and lymph nodes of cattle which are not found in the liver, kidneys or muscle and possess a characteristic action. The one of these substances prepared from cattle spleen lowers the serum calcium in the typical clinical picture; the other lowers the content of the serum in inorganic phosphorus.

Spasms of the Esophagus and of the Cardia.—J. Pal. (*Wien. klin. Wochenschr.*, **42** : 765, 1929.)

A possibility of influencing spasm of the esophagus with adrenalin is given. In the beginning adrenalin has a dilating action on the cardia spasm through stimulation of the sympathetic even when subcutaneously used. It is important therapeutically that a few drops of adrenalin introduced into the esophagus immediately before meals, temporarily induce permeability. This is not only possible in stenosis but even in carcinoma. The author was repeatedly able to maintain the stenosis (in stenosis of the esophagus conditioned by carcinoma) permeable to such an extent with adrenalin that feeding was possible or a sound could be introduced. This would be of especial advantage for the treatment if it were possible to lessen the tension locally through medicaments. Such a medicament is not yet known.

Testicular Insufficiency Due to Double Congenital Microorchidism; Grafting by Voronoff's Method; Result. — Delaren and Muller. (*Presse méd.*, **37** : 838, June 1929.)

The subject, a man aged 42 years, affected with double congenital microorchidism, presented physical, psychic and sexual signs of testicular insufficiency. In May, 1928,

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patient underwent a transplantation operation of a cynocephalus monkey according to Voronoff's method. The result 1 year later is remarkable from three viewpoints: (1) Physical (disappearance of asthenia and muscular fatigue, greater aptitude for prolonged work, beginning appearance of secondary sexual characters, hair of mustache and beard, pubic hair). (2) Psychic (sense of well being, changes in disposition in masculine sense) and (3) sexual (greater frequence of erections followed by ejaculations).

Ways of Activating the Formation of Callus in Fractures of the Bones. — K. Glaessner and J. Hass. (*Presse méd.*, **37** : 176, Feb. 6, 1929.)

The authors studied the influence of the thymus and thymus extracts on the consolidation of fractures in young cats. They found that extirpation of the thymus causes a retardation in formation of callus and that extract of thymus accelerates the evolution of fractures. In a second series of experiences they compared the activity of different glandular extracts: injection of albumin, testicular extract, parathyroidin and extract of thymus. Thymus extract had the greatest action on the ossification of the callus. Even parathyroid extract (Collip's) had an action very much inferior to that of thymus extract.

In man thymus extract likewise induced an acceleration in the consolidation of fractures. The medicament can be absorbed in large doses without danger. The authors chose two subjects of almost the same age, in whom they practised a linear osteotomy of the two femurs for defects of osseous formation. In one of the cases they injected thymus, there was no difference at the end of 4 weeks. At the end of 3 months the differentiation was great. The patient who had not received thymus still presented mobility, and radiography with difficulty revealed the existence of a callus. On the other hand the patient who had received thymus extract had a completely consolidated fracture and the callus was solidly formed of medullary substance as well as of osseous compact. This experience leads to the conclusion that thymus extract also activates the formation of callus in man. Since then the authors have studied the action of thymus extracts in a series of cases of retardation of consolidation. All these experiments permit the conclusion that thymus extract combined with a phosphorated substance gives a rapid consolidation of fractures not only in animals but also in man.

Concerning the Heart Hormone of Haberlandt. Report Concerning the Sessions of the Moscow Division of the Russian Pathological Society. — Pawlenko. (*Centrbl. allg. Path. u. path. Anat.*, **45** : 272, 1929.)

The analysis of the substance designated as heart hormone convinced the author (in contrast to Haberlandt) that the extract of the auricle and ventricle exerts an identical action on the isolated heart. The skeletal musculature and a simple Ringer-Locke solution which contains albumin in traces, are identical in action. It was, moreover, established that albumoses, peptones and amino-acids in definite concentration and mixture influence the heart in quite the same way as does the substance designated heart hormone by Haberlandt. Accordingly, it must be assumed that a specific heart hormone does not exist. The action of the aqueous extract of the heart musculature is determined by the albumin products of disintegration contained in it and extractive substances.

Generalized Atrophic Scleroderma with Ovarian-Mammary Syndrome (Genito-Sclerodermic Syndrome) of Tuberculous Origin. — F. Trémolières, J. Lhermitte, A. Tardieu and A. Carteaud. (*Presse méd.*, **37** : 883, July 6, 1929.)

The patient, a young girl of 19 years, was affected with a generalized atrophic scleroderma the evolution of which was regularly progressive and terminated in cachexia and death within about 3½ years. The onset of the scleroderma coincided with the total suppression of the menstrual function and with atrophy of the breasts.

From the histological viewpoint the skin underwent the alterations described under the term of atrophic scleroderma. The sclerosis was complete in the ovaries and breasts and the glandular elements had disappeared. The cortical substance of the kidneys was likewise affected by a marked sclerosis.

This example of the association of scleroderma with ovarian-mammary syndrome enters into the picture of the pluriglandular syndromes which characterize the period of pubertal evolution.

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The authors admit that in this case the scleroderma and the sclerosis of the ovarian and mammary glands, the renal sclerosis, are the expression in the different organs of an identical morbid process set in action by the same etiologic factor: tuberculosis. At autopsy the authors discovered a large bacillary adenopathy next to the pancreas, verified histologically, which remained latent and which was but indirectly manifested by cutaneous and glandular alterations.

Concerning the Place of the Ovarian Hormone in the Hormone Series. — K. Csepai, A. Fornet and St. Pelláthy. (*Endokrinologie*, **3** : 361, 1929.)

The authors have undertaken the investigation of the effect of the ovarian hormone on human beings and tested the action of this hormone on blood pressure, on true adrenalin sensitiveness, on the sugar and calcium content and on the reaction of the blood under diverse circumstances. The following was the result. The ovarian hormone lowered the blood pressure in the majority of the cases even if not significantly. This effect was most significant in some cases of high blood pressure in which within ½ to 1 hour the blood pressure fell from 20 to 25 per cent.

The adrenalin sensitiveness was lowered in almost all cases under the action of the ovarian hormone; still the hormone does not apparently exert so uniform an action in women as in men. The ovarian hormone acts depressing on the tonus of the sympathetic; cases of menstruation and pregnancy form an exception.

In four of nine cases a marked fall of blood sugar picture was perceptible with the ovarian hormone. The action is still more intensive with intravenous administration; but is not significant (max. 0.05 per cent). Moreover, the ovarian hormone lowers the blood pressure. Investigations of the blood pH gave negative result in seven cases.

A Suitable Combination for the Control of the Asthmatic Attack and of Other Allergic Diseases. — M. J. Gutmann. (*Die med. Welt*, **3** : 751, 1929.)

Through the combined parenteral use of ephedrin with suprarenal hormone a remarkable expansion of the treatment of asthma has been accomplished. Whereas the internal administration of ephedrin has been found to be of practical value and very comfortable for the patient and has favorably influenced the asthmatic condition and the interval between the attacks can be widened, the advantage of ephedrin can also be utilized now in the severe acute attack of asthma in that it can be used in injections in combination with adrenalin. The amount of adrenalin in this combination preparation must be chosen so large that it renders possible a complete control of the attack: that is in the majority of cases 0.2 to 0.3 cc. of the solution 1:1000. The action must continue until the action of ephedrin appears. Ephedrin thus prolongs the action of adrenalin, averts the danger of fall of blood pressure below the terminal point and gradually wears away.

Concerning the Hormone of Heart Movement. Pharmacological Investigations with the Heart Hormone Preparation. — L. Haberlandt. (*Pflügers Arch. ges. Physiol. Mensch. u. Tiere*, **222** : 259, 1929.)

Through preliminary treatment with heart hormone preparation the action of digitalis glucosides (strophanthin, digipuratum and squill) on the isolated frog heart beating in the Straub cannula is distinctly heightened. This sensitizing action has already been demonstrated clinically. The resistance of the isolated frog heart placed on the Straub cannula to chloroform and ether anesthesia may be essentially increased through the same preliminary treatment with the heart hormone preparation.

Concerning Organotherapeutic Preparations in the Pharmacopoeias and Their Methods of Investigation. — K. Neumayer. (*Arch. Pharm. u. Ber. deut. pharmacol. Ges.*, **267** : 27, 1929.)

The pharmacognostic methods of investigation of organ preparations outside of thyroid and suprarenal the active principles of which have already been conceived in part, meet with great difficulties. Specific chemical reactions are lacking and the identity and purity of the individual preparations are principally to be determined through biologic reactions. The determination of physico-chemical constants, such as dry residue, ash content and extract content must also be desired for the remedies. For some time past works of this kind have been carried on in the pharmacognostic institute of the University of Vienna and microscopic investigations are being made for the determination of the structure

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animal drug preparations from desiccated animal organs and the possibility of a differentiation in this way was tested. Next the source of the desiccated preparations was investigated. A method was also found to prepare microscopic sections of organs in powder form. The microscopic investigation of the sections obtained in this way gave the possibility of differentiation of various cell types. As example of the microchemical characterization the author reports concerning a qualitative demonstration of iodin from thyroid substance.

Ovarian Hormone and Basal Metabolism. — G. Koehler. (*Klin. Wochenschr.*, 8 : 502, 1929.)

As criterium for the activity of the ovarian hormone the determination of the gas exchange has become of great significance. In their castration experiments Loewy and Richter found a fall of O_2 consumption of about 15 per cent following deficiency of sex gland function, which they could again adjust by administration of specific ovarian substance. Since these observations were reported, the determinations of basal metabolism have also been undertaken during the menstrual cycle, in conditions of ovarian insufficiency or following administration of ovarian substance, and there are numerous experimental and clinical investigations on the subject.

The results of these investigations by Heyn, Klaften and Hornung show that the cyclic processes of ovulation and of menstruation exert no direct influence on the basal metabolism. The above mentioned authors could also determine a slight fall of basal metabolism in mild forms of ovarian insufficiency as well as at the time of the climacteric and following surgical or x-ray castration only in isolated cases, whereas the greater number were associated with normal or slightly raised gas exchange. Lüthje came to the same results.

As regards the investigations concerning the ability of the basal metabolism to be influenced by administration of ovarian substance, a not inconsiderable rise of basal metabolism (of 6 to 23 per cent) was obtained by Brugsch and Rothmann, Heyn, Hannes). Recently at the suggestion of Prof. H. Zondek, in a great number of patients with visible signs of disturbed sex gland function, the authors attempted to influence the gas exchange with ovarian preparations. For these experiments they used the ovarian hormone prepared by B. Zondek and Aschheim in water-soluble form, the activity of which had been demonstrated on the basis of test methods used.

From tables given in the original article it is to be seen that the authors could not discover any influence of administration of ovarian hormone on gas exchange in any of the cases investigated. The fact that in countless cases of objectively visible disorders of the sex glands function, as for example in obese castrates, the author was not successful in raising the gas exchange by ovarian hormone administration or in obtaining an increase in weight, should be a proof for the fact that the sex glands have only a slight importance or none whatever for the occurrence of obesity, and that for this purpose pituitary and thyroid must be ascribed the dominant rôle as regulators of the economy of the organism. It is to be assumed that the adiposity appearing after castration is not directly caused by loss of the sex glands, but arises by way of secondarily induced changes in the pituitary or thyroid.

A Case of Pituitary Dwarfism. — G. Roussy, J. Bollack and N. Kyriaco. (*Rev. neurol.*, 1 : 102, No. 1, Jan., 1929.)

The rarity of cases of pituitary dwarfism induced the authors to report the case of a patient in whom the syndrome was especially distinguished and perhaps connected with a lesion of the pituitary. The patient was a little girl of 12 years, born at term of healthy parents. She has a brother, 18 years of age, normally developed. The onset of the present syndrome dates back to August, 1926, when the child's mother noted a decrease in vision of the right eye with slight strabismus on that side. In March, 1928, the child remarked that the right visual field was diminished more and more. A diagnosis of chiasmic compression was made and immediately directed attention to the arrest of development of the child, manifested for the past 3 years. The authors were struck by the slight size of the girl, who was no taller than a child of nine years. The facies was slightly swollen, the skin of the face and of the whole body was a little dry with tendency to ichthyosis; slight hyperkeratosis of the hairy system was present in the region of the extremities. The hair was also dry. The secondary sexual

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characters were lacking although the child was still very young (12 years). Otherwise there was no disturbance. Her intelligence was especially well developed for her age. She was very affectionate and agreeable. Radiography of the skull showed a considerable enlargement of the sella turcica. Radiography of the various articulations of the extremities showed that there was no retardation of the ossification. General examination revealed nothing in particular. All the reflexes were normal. The child presented no sign of intracranial hypertension: no diffuse or localized headache; no vomiting or nausea; no somnolence. All tests for the study of pituitary syndromes were negative. There was no sugar nor albumin in the urine.

Summarizing, the clinical picture of pituitary dwarfism was complete. The radiographic findings (sella turcica increased in all its dimensions with integrity of the clinoids), the visual disorders (almost complete blindness owing to optic atrophy on the one side; temporal constriction of the other side), gave confirmation to this diagnosis. From the viewpoint of pathological physiology it is therefore a question of a syndrome through affection of the anterior lobe of the pituitary, a syndrome whose pathogenesis is still rather obscure and which should be placed along side of other great osseous syndromes of the anterior lobe: gigantism and acromegaly. The case resembles to a certain extent those reported under the name of pituitary infantilism. It also resembles cases of pure dwarfism without infantilism. Owing to the age of the little patient it is impossible to decide the state of development of the genital organs and of the secondary sexual characters. It is, therefore, difficult for us to say whether or not it is a question of dwarfism associated with infantilism. It is also difficult to determine the nature of the tumoral lesion which has brought about the enlargement of the sella turcica and the affection of the chiasma respecting wholly the nuclei of the tuber. It may be an adenoepithelioma arising in the sella turcica and involving the chiasma directly or by intermediary of the anterior communicant or it may be one of those cystic or solid tumors developed at the expense of Rathke's pouch. This latter hypothesis appears most probable. A course of treatment with deep radiotherapy was begun but is so recent that the authors are unable to judge of its effect. According to the result obtained the authors will decide whether surgical treatment is to be thought of.

Basal Metabolism. — H. Janet. (*Monde méd.*, **39** : 640, 1929.)

Not infrequently small goiters without any symptom of a hyper- or hypo-thyroidism are observed in children. The determination of the basal metabolism may be important therapeutically in such cases. In such a case in a small girl who was apathetic, and remained backward in school, etc., the author obtained a very essential improvement in spirits and in the symptoms mentioned by long continued thyroid therapy.

Hyperthyroidism and Insulin Sensitiveness. — E. Adler. (*Wien. Arch. Med.*, **16** : 343, 1929.)

Repeated blood sugar determinations following subcutaneous injection of 5 units insulin did not show any difference in insensitivity between normal individuals and patients with hyperthyrosis. Between cases of more severe and milder hyperthyrosis essential difference in the sensitiveness insulin was recognizable. Fixed relations between rise of basal metabolism and insensitiveness are likewise not present.

Preparation of Two Active and Specific Thymus Substances, Their Influence on Calcium and Phosphate Content of Rabbit Serum. — A. Nitschke. (*Zeitschr. exp. Med.*, **65** : 637, 1929.)

The significance and function of the thymus are still very slightly known. Hammar and Gley are in doubt as to the presence of an internal secretory gland. Thomas considers all influence of the thymus on the metabolism as unproved. The author made investigations on rabbits with acetic-aqueous and acetic-alcoholic extracts of thymus. Following one or for the most part two injections a marked fall in blood calcium content occurs with severe tonic-clonic convulsions. The author believes that the fall in calcium is effected by a substance characteristic for the thymus which probably is to be regarded as the internal secretion of the gland. The characteristic symptom in tetany — the neuro-hyperexcitability — could also be demonstrated on the animals.

Other experiments with extracts prepared according to definite method, yielded a se-

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substance likewise with greatest probability specific for the thymus, which lowers the inorganic phosphate of the serum. The calcium lowering principle is water-soluble, acid- and alkali-resistant and resistant to heat. The phosphorus lowering principle is resistant to acid, alkali and heat; it is, however, insoluble in purely aqueous solutions. The thymus must be ascribed a hormonal influence on phosphate metabolism. Important questions are disclosed in this way for pediatrics.

Non-Specific Stimulating Therapy with Insulin and Glucose Forced Feeding Treatment in Chronic Pulmonary Tuberculosis. — H. Bergmann. (*Die med. Welt*, 3 : 726, 1929.)

Report concerning 8 cases of tuberculosis treated with insulin. In two cases the treatment had to be prematurely interrupted, since despite careful asepsis at the site of injection, infiltrates originated. On the whole the reports in the literature up to the present, concerning the value of an insulin forced feeding cure in tuberculosis, as well as in severe diseases, which received a careful dosage, are corroborated.

Endocrine Gigantism and Dwarfism. — M. Berliner. (*Zeitschr. ärzt. Fortb.*, **26** : 352, 1929.)

In forms of dwarfism, with exception of chondrodystrophy, very fine results are often to be obtained through the administration of the deficient hormone, especially in myxedema. Perhaps these are to be explained by the fact that under the influence of the hormone administered, the gland itself may be stimulated to renewed effort. In gigantism conditioned by the endocrine glands, the height can be restrained in some cases by ovarian or testis preparations.

Action of Placenta Extracts on pH of the Blood. — Imparato. (*Paris méd.*, **19** : 500, 1929.)

In previous communications the author has shown that intravenous injections of folliculin and pituitary anterior lobe occasion alkalosis whereas corpus luteum and pituitary extract cause acidosis. In the present communication it is reported that the results obtained with injection of placenta are uncertain, yet in the majority of cases they occasion alkalosis.

Insulin Treatment of the Fistulae Following Gastric Operations. — A. Lupan. (*Zentrbl. Chir.*, **56** : 1423, 1929.)

In several cases of fistulae of the duodenum, stomach and intestine following gastric resection, injections of insulin were made. The results obtained were very satisfactory since in the shortest possible time a cure of the fistulae and recovery of the patient was attained. The favorable effect of insulin is to be explained by the fact that it is a hormone which activates the basal metabolism of the cell, etc., through marked oxidation of the carbohydrate. The cells get back their vitality whereby a more rapid healing of the wound is obtained.

Report Concerning Results Which Were Obtained with Pituitary Substitution Therapy. — K. Ehrhardt. (*Zeitschr. Geburtsh. u. Gynäkol.*, **95** : 378, 1929.)

In a 61 year old patient with pituitary cachexia the author obtained an increase in weight of 20 pounds, growth of axillary hair and restitution of working capacity within 2 months with pituitary anterior lobe therapy. In other cases Ehrhardt observed fine results from substitution therapy by means of transplantation of anterior lobe of sterilely removed pituitary of cattle in adiposogenital dystrophy and amenorrhea. It was further reported that the pregnancy reaction reported by Zondek and Aschheim was tested in 200 cases and could be entirely corroborated.

Myopathies and Endocrine Disturbances. — On the Subject of a Clinical Observation of Non-Familial Myopathy of the Loeden-Moebius Type with Pluriglandular Symptom Complex. — L. Langeron, R. Caliegue and P. Duquesne. (*J. Méd. Lyon*, **10** : 369, 1929.)

The determination of more or less distinct endocrine disturbances in connection with myopathy in several cases logically led to the trial of an organotherapeutic treatment of the disease. The therapeutic experiment had a very unsatisfactory result. Pituitary, thyroid, thymus, suprarenal, testicular extract and pluriglandular therapy were tried. In the best case a functional improvement was obtained but never a disappearance of the muscular atrophy or a fixation of the atrophic process.

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Concerning the Action of Adrenal Cortex and of Histamin on the Blood Cell Regeneration. — E. Huth. (*Wien. klin. Wochenschr.*, **42** : 739, 1929.)

The author carried out a treatment with adrenal cortex and histamin in more than 60 patients with anemia. Both preparations were found to be of equal value to liver with regard to the regeneration of blood cells. In addition to increase of blood cell count there was regularly shown increased appetite and as a rule also increase in body weight. Four cases of pernicious anemia which had been under liver treatment for weeks in the hospital were changed to treatment with histamin for 3 weeks. The increase of erythrocytes, the improvement of appetite and of the general condition continued as if no change had been made in therapy. Other patients suffering from pernicious anemia received histamin exclusively from the first day of hospital treatment. The results corresponded to that of liver treatment.

Concerning the Morphology of Experimental Hyperthyroidism. The Endocrine System of the Organism in the Act of Growth in Systematic Feeding of Thyroid Substance. — E. Kliwanskaja-Kroll. (*Virchows Arch. path. Anat. u. Physiol. u. klin. Med.*, **272** : 430, 1929.)

In the feeding of rats with thyroid substance the first marked changes in the thyroid appeared after 30 days of feeding. The changes are all the more marked the longer the period of feeding. The cell changes refer to a suppression of gland activity. The hyperthyroidism artificially induced through feeding with desiccated thyroid substance was followed by hypertrophy of the thymus — of its parenchyma. The increase of cortical layer exceeds that of the principal medullary layer. The number of Hassall's bodies is markedly increased in the thymus of the experimental animal. An increase of the thymus may be observed (10 days of feeding with thyroid).

The Alkalin Reserve in Animals Subjected to a Thyroid Treatment. — C. J. Parhon, M. Cahane and J. Orenstein. (*Compte rend. séances soc. biol.*, **101** : 231, 1929.)

The observations relate to 8 full grown dogs who received 2 to 4 gm. desiccated thyroid daily for 27 to 34 days. The hyperthyroidization attained could be demonstrated [illegible] the loss in weight of the animals [illegible] amounted to 3 to 4 kgm. The alkali reserve was determined according to Van Slyke. [illegible] all, 154 determinations were made. From [illegible] investigations it is shown that the alkali reserve is lowered in hyperthyroid animals which is manifested in a tendency to acidosis. Saida determined the same diminution of the alkali reserve in clinical observations.

Neuroanemic Syndrome with Optic Atrophy. Failure of Liver Treatment. — J. Dereux. (*Bull. et mém. Soc. méd. Hôp. Paris*, **45** : 577, 1929.)

Whereas several authors, as for example Crouzon, P. Mathieu and Gilbert-Dreyfus, as well as Paul Jacquel and Desbuquois have reported recovery of patients in cases of neuroanemic symptom complex by use of Whipple's method of treatment, the author treated one case in which this therapy failed. It is emphasized that in treatment according to Whipple, it is a question of dissociated treatment. The therapy influences the anemic process but has no influence on the further development of the neurologic process. This observation is not surprising for liver therapy may not get at the basic causes of the disease. P. E. Weil and Picard also have reported concerning this dissociation of action of liver therapy.

Concerning the Hepatic Point of Attack of Insulin. The Primary Paradoxic Insulin Hyperglycemia. — M. Bürger and H. Kramer. (*Zeitschr. ges. exp. Med.*, **65** : 45[illegible] 1929.)

The intravenous injection of insulin regularly results in an initial hyperglycemia in man and dogs. The intraportal injection of insulin shows in dogs increase of blood sugar up to 100 per cent, on the average 33 per cent. Following interruption of the liver circulation the primary insulin hyperglycemia remains absent. The primary insulin hyperglycemia is to be obtained with all types of insulin tested. It is a physiological manifestation.

Treatment of Diarrhea Due to Insufficiency of the Digestive Glands. — (*Progrès méd.*, **57** : 969, 1929.)

According to the etiology, treatment must in part be a substitution organotherapy and in part an organotherapy stimulating secretion

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In gastric insufficiency the organotherapeutic measure consists in the administration of natural gastric juices which are prepared under various names and in part in the administration of gastric extracts which contain a hormone (secretin). In pancreas insufficiency it is always to be noticed that pancreas organotherapy acts only in alkalin medium. Pancreas extracts, powder or solution are used. A combination of pancreas with malt can also be given. In manifestations of liver insufficiency, liver preparations in the form of extracts, tablets or fluid extracts come into consideration.

Castration in Pregnancy. — J. Halban. (*Wien. klin. Wochenschr.*, **42** : 697, 1929.)

The corpus luteum has no significance for pregnancy in the human being. Waldstein's investigations show that in pregnancy the placenta produces the ovarian hormone. The fetus does not come into consideration as source of the hormone, since also in cases of cystic mole and stillbirth, the production of hormone is not disturbed.

The Treatment of Arterial Hypertension. — E. Donzelot. (*Le Monde méd.*, **39** : 481, 1929.)

The organotherapeutic treatment of these disease cases can under certain circumstances attain the value of an absolute causal therapy. This is especially the case in organotherapy with ovarian preparations in the course of hypertension of the menopause. Thyroid therapy also, the field of indication of which is extensive, was proposed in small doses (in milligrams and parts of milligrams). This therapy should give encouraging results at times. A substance which deserves much greater interest than those mentioned hitherto is a pancreas preparation. The hypotensive even if not regularly appearing action of this pancreas extract has already been mentioned by various authors; Kisthinios has shown that this pancreas extract can not only cause a fall of blood pressure but can also neutralize the action of adrenalin. Gley and Kisthinios have recently succeeded in showing that the pressure-lowering and blood sugar-lowering action of a given pancreas extract are independent of one another and they even succeeded in isolating a substance from the pancreas which merely acts by lowering pressure. The injection of this substance makes superfluous a series of precautionary measures which are otherwise necessary, so that a great stride is made in therapy through this. Clinically, it is not yet possible to exactly limit the manner of action and field of action of this special pancreas extract. In any case the administration of this is simple and its use is indicated in particular in those cases of hypertension in which anginous pains appear.

Obesity Through Endocrine and Psychogenic Bulimia. — E. Bonilla. (*Med. Ibera*, **24** : 727, June 1, 1929.)

The patient is a woman of 34 years. Her mother was very fat and so are all the relatives on the maternal side. The patient has always been stout, but not excessively so. Menstruation at 13 years. Flow somewhat scant. Within the last 2 years, amenorrhea for 4 months. She has been married 11 years: had 4 children. Her present illness began during the last pregnancy 1 year ago with great emotionalism, insomnia and sensation of anguish and great hunger. The crises of weakness increased still more after delivery and her great obesity then developed. At the beginning of pregnancy, she weighed 85 kg.; at the present time, 119 kg. Examination of the patient revealed a very great generalized obesity. Basal metabolism was +9 per cent. Mental examination showed that the patient was a marked oligophrenic (torpid imbecile). She was subjected to treatment with thyroidin (4 tablets daily) and restricted diet. Within 2 months, the patient left the clinic with a weight of 124 kg. and a basal metabolism of +9 per cent.

The author believes as does Marañón that every treatment of obesity is mixed; exogenous factors (hyperalimentation, sedentary existence) and endogenous factors (thyroid, neuropituitary, genital, etc.) intervene. Great importance is given to the intervention of the pancreatic factor in the pathogenesis of obesity. The magnificent results obtained with insulin in states of emaciation have changed the conception that insulin insufficiency would cause an excess of carbohydrate to be stored in the organism as fat. Falta maintains that only those individuals can grow fat who possess a normal island function. When this is exaggerated the patients suffer a rapid ontake of fat; but the excess work of the pancreas finally exhausts it, giving rise to prediabetic states and confirmed diabetes. Recently, there have been described

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in the clinic spontaneous hypoglycemic syndromes analogous to those induced by insulin. These syndromes which almost always appear in laborers are characterized above all by crises of great hunger during which the glycemia is very low and which disappear with the administration of food particularly sweets. These crises are induced by a hyperinsulinism. According to Fonseca, hyperinsulinism is constant in obesity. Sometimes it is due to a greater production of insulin and at others to the lack of antagonistic hormones of the pancreas which correspond to thyroid, pituitary and genital obesities; but it is always the insulin which determines the obesity through its fattening effect. This idea alters the one classically admitted concerning the intervention of the genital glands in an identical sense as that of the pancreas in carbohydrate metabolism, based on the greater frequency of diabetes in the climacteric and the facility of inducing spontaneous, alimentary and adrenalin glycemia in castrated animals and women and in the critical age. The changes recently encountered in the pancreas of castrated animals and the hyperglycemic effect of ovarian extracts make one believe that the genital insufficiency induces a hyperinsulinism which causes the obesity. It is very possible that this is so and that the glycosuria of castrated animals and the coincidence of diabetes with the critical age is due to the hyperfunctional reaction of other glands, especially suprarenals which turn the carbohydrate metabolism in the diabetic direction.

All the facts related by the author demonstrate that the insulin hormone plays a primary rôle in those states in which the processes of assimilation are increased. It is more difficult to determine whether there are treatments for obesity whose cause resides in a primary insular activity, either through conditions in the pancreas itself or through an abnormal excitability of the hypothalamic nervous centers, regulating endocrine pancreatic activity. The author's patient appears at first sight to be a typical case of exogenous obesity, induced by excess of food intake consequent to her mental state, although the hereditary antecedents and her slight ovarian insufficiency suggest the existence of predisposing endogenous factors. The great similarity of the clinical picture with the one described by Harris and others, inclines the author to believe in the intervention of a hyperinsulinic factor. In the author's opinion, the fall of the blood sugar curve after 2 hours indicates a hyperactivity of the endocrine tissue of the pancreas.

Some Considerations Concerning a Case of Pseudo-Hermaphroditism in a Woman. — S. Recasens. (*Med. Ibera*, 24 724, June 1, 1929.)

The patient presented a peniform clitoris 2 cm. long in flaccidity, and 5 cm. in erection, two swellings resembling testes, one situated on the left labia major, painful to pressure, and the other located in the right inguinal ring. There was an opening in the external genitals at certain distance from the clitoris through which the patient urinated and menstruated. It is a case of pseudo-hermaphroditism because the patient has masculine characteristics. This woman also presented a sarcoma of the ovary. After surgical intervention, it was seen that the sarcoma was located in the ovary with its normal tube. At the same time the two tumors were extirpated. Analysis of these tumors showed that one in the right inguinal passage was a cystic hydrocele; that of the left labia major showed a histological constitution resembling that of an ovarian cyst if on closer examination it does not prove to be a more or less altered masculine genital gland.

Endocrine Rheumatism. — S. Pueyo Veloso. (*Arch. Med. Cir. y Especialid.*, 30 685, June 8, 1929.)

The author draws attention to the endocrine alterations and the importance they have in many cases of rheumatism. Hyper- hypo- or a-function of the thyroid and ovaries, principally ovary in the female sex, is the determining factor in the rheumatic crises. These endocrine disturbances in the majority are manifested by trophic disorders, fragility of the nails, vasomotor excitability, tendency to sweating; all depend on thyroid and ovarian dysfunction. In women affected with acute articular rheumatism disorders of the genital tract are often noted, with dysmenorrhea, genital aplasia, with initial menstrual retardation.

Ardillier and especially Leriche have observed the relation between rheumatic pain and ovarian castration. These painful crises which the author was able to observe, precede the menopause and exacerbate when the menopause occurs and even after the meno-

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pause, affecting all the articulations but especially the metacarpo-phalanges and the knees. Sometimes, in patients with rheumatic crises the pains are manifested during the menstrual period after being absent or at least faint before the period. It is interesting to note that women affected with vagosympathetic disequilibrium are most predisposed during the critical age to develop rheumatism. In one patient with a bilateral tuberculous process with rheumatic disturbances, the author was able to follow the evolution of her pain, noting that this exacerbated during the menstrual period and in the 2 months when her period did not appear these crises were of greater intensity, disappearing with thyro-ovarian therapeusis.

Many patients with rheumatism are suffering from thyroid disturbances but in the author's opinion, in the woman, the ovary is the gland which has an intimate relation in many cases to the painful crises. He reports four cases in point.

Antagonism Between the Different Substances in the Pituitary and the Action of Insulin in Normal Dogs and Hypophyseopriva Dogs. — M. A. Magenta. (*La Semana méd.*, **36** : 1275, No. 20, May 16, 1929.)

The oxytocic principle (oxytocin) of the extract of posterior pituitary is the active part in the insulin-pituitary antagonism. The hypertensor principle (vasopressin) does not modify the hypoglycemic action of insulin. An extract of anterior lobe prepared according to technique of Putnam, Teel and Benedict also fails to modify the action of insulin. Oxytocin causes a disappearance of the convulsive symptoms and raises the glycemia of hypophyseopriva dogs in insulin hypoglycemia.

The Antagonism Between the Pituitary and Insulin in Toads. — B. A. H. Houssay and D. Potick. (*La Semana méd.*, **36** : 1275, No. 20, May 16, 1929.)

The injection of insulin into toads 24 hours before injection of extract of posterior lobe of pituitary decreases the action of this extract on absorption; it has little or no effect on the oliguric action of the extract; the two substances dilate the melanophores and their effects are united. Extirpation of the pituitary increases considerably the sensitiveness of the toads to the toxic action of insulin. Extirpation of the anterior lobe only also increases this sensitiveness but in a less degree.

Infundibulo-tuberian lesion does not modify the sensitiveness of toads to insulin. Extract of anterior lobe and of posterior lobe and daily implantation of anterior lobe correct hypersensitiveness of the hypophyseopriva toads. The daily implantation of posterior lobe (intermediate part and nervous) does not produce this effect.

Hypothyroidism Accompanied by Various Neurologic Disorders. — Zygmunt W. Kuligowski. (*Rev. neurol.*, **1** : 514, No. 3, Mar., 1929.)

A female patient of 58 years presented signs of thyroid insufficiency: edema, dryness of the skin, lowering of basal metabolism, flattening of the P and T, waves of the electrocardiogram, slowing of cardiac contractions on radioscopy, increase in amount of albumin in the serum up to 10.25 per cent; diminution of urine, suppression of sweat, chilling, insensibility with regard to vegetative poisons, slowing of movements, slight hebetude. At the same time the patient presents a series of neurologic symptoms of undoubted organic origin.

After treatment with thyroidin for a week, the signs of thyroid insufficiency disappeared; the neurologic signs subsided in part, with the exception of the fixed facies and the absence of Achillean reflexes. The Wassermann test was slightly positive in the blood so thyroid treatment was interrupted to institute specific treatment: it was without effect on the nervous system and the hypothyroid symptoms reappeared. The author believes accordingly that these nervous symptoms are dependent upon the hypothyroidism.

Deviation of the Endocrine Glands as Method of Treatment in Atrophy or Underdevelopment. — J. A. Goljanitzki and A. L. Obolenskaja. (*Arch. klin. Chir.*, **154** : 623, 1929.)

Organotherapy can lead to only one result, when the corresponding brain centers and the vegetative nerves controlled by them can still respond to the stimulus. In centrally conditioned atrophy this therapy proves to be completely powerless. Characteristic for cerebral conditioned atrophies is their polyglandular character and the extensive dis-

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turbance of metabolism. It is clear that organotherapy is condemned to failure in extinguished ability to react on the brain and vegetative nervous system. The attempt to do away with insufficiency of the endocrine glands through a transplantation depends on just as false a presupposition as the "rejuvenation" of these glands through destruction of their excretory portion. On the other hand, there exists the possibility in more or less peripherally conditioned atrophies and aplasias of the endocrine glands to again restore the glands through their reversing to new blood and nerve paths.

The author reports concerning successful interventions in myxedema and in sex gland atrophy.

Concerning the Field of Use of Ovarian Preparations. — Schröder. (*Münch. med. Wochenschr.*, **76** : 84, 1929.)

The ovarian preparations must be tested on well chosen cases. Deficiency symptoms in normal or artificial climacteric are no suitable field. Non-specific preparations also suffice here in addition to those which have always been on the market. Old hormone defects arising secondarily following general disease of the body or directly following pelvic inflammations are not suitable for hormone therapy but only such insufficiencies which may be recognized as obviously located primarily in the ovary.

Interrenal Syndrome. Precocious Menopause, Hirsutism, Virilism, Pseudo-Hermaphroditism. Hypernephroma of the Left Suprarenal Gland. Confirmation of Clinical Diagnosis by Necropsy. Sclerosis of the Thyroid Gland, Climacteric Ovaries. — Syllaba and V. Jedlicka. (*Rev. neurol.*, **1** : 525, No. 3, Mar., 1929.)

The patient was a woman aged 38 years. Normal development of physical and psychic strength during childhood before and after puberty. Married at 29 years, the patient gave birth to two children. At the age of 36 years, menstruation ceased and 1 year later she also lost the orgasm during coitus. At this time she became transformed in external appearance. Her voice became hoarse; her hair crisp, the limit of the hair on her forehead was replaced by appearance of angles of alopecia on the forehead; a mustache developed on her lips and a beard on her chin; the shoulders enlarged. The breasts disappeared and the pubic hair became strong. At the same time the patient became altogether cold in her sexual relations and even in her maternal love she neglected her children. In the course of the last month terrific pains in the back and in the sacral region. The patient grew weak; she became bedridden for the past 3 months. In December, 1928, she had quite a virile appearance in face, head and trunk. The clitoris is 3 cm. in length, with a duplication of the skin. In the left epigastrium there was a tumor and under the tumor the kidney was found. In the inguinal region there was a metastasis and in the left pleural cavity a hemorrhagic effusion.

The author questions whether virilism and hirsutism are due to dysfunction of the suprarenal cortex or according to Falta to a hyperfunction. The patient died January 17, 1928, and V. Jedlicka presents the microscopic preparations. A cortical adenoma composed of young eosinophil cells of large dimensions emerged from the left suprarenal, its metastases into the lymphatic glands and into the left pleura. The right suprarenal was small with the cortex very much reduced, with the medulla hypertrophic; in the thyroid there was a fibrous sclerosis; in the ovaries a precocious climacteric appearance whereas the thymus was completely involuted.

In the discussion M. Pelnai recalls the varied combinations and atypical forms of the interrenal syndrome. There are interesting combinations of beard formation and of virile form of disposition of pelvic hair, that is, in triangle. He mentions two similar cases in his clinic, in which this partial masculinization appeared at puberty, 1 to 2 years after the appearance of menstrual periods which were regular or postponed but always with hyponormal menstruation; the ulterior physical and psychic evolution was normal. The beard appears rather frequently in the menopause, but it is not known whether it combines with the virile type of arrangement of hair or whether it is merely a senile hirsutism. These partial pubertal masculinizations are certainly not conditioned by a simple ovarian hypofunction; it is probable that it is a question of change of interrenal function but in opposition to the present case it is a question of temporary pubertal disturbance.

M. Bondy recently examined a singer of 36 years, well developed as a woman; nevertheless, for

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less, for some time past a mustache and beard have appeared; menstruation has disappeared and the hair has fallen out and become coarse. There is also a masculine type of arrangement of pelvic hair but no mental change. The most disquieting disorder for a singer is a hoarse voice which accompanied all these changes.

M. Jedlicka has examined several cases of senile beard in women: the suprarenals were always normal and the arrangement of the hair was of feminine type.

Case of Tumor of the Pituitary in a Dwarf. — K. Poncz. (*Rev. neurol.*, **1** : 515, No. 3, Mar., 1929.)

The patient is 34 years old, married. Absence of menstruation for the past 6 years, and of the sexual desire with abnormal obesity. Three years after onset, transient polyuria. For the past 8 months, decrease of vision and headache in the frontoparietal region. Two healthy children, three miscarriages. Parents were of small stature as well as an older sister. The patient under treatment is a dwarf (1.33 m. in height). She is pale, her thyroid is not perceptible. The adipose pannicle is very much developed. Percussion of the forehead is painful. Examination of the fundus of the eye shows slight atrophy of the right optic nerve. Visual acuity on the left: 1/24. On the right, 1/60. Bitemporal hemianopsia. Arterial tension 9 to 5. The ovaries are small; the mammary glands but slightly developed; there is no axillary hair, but little on the pubis. The radiograph of the skull shows an enlargement of the bottom of the sella turcica, the back and posterior clinoid apophyses are injured. A diagnosis of tumor of the pituitary was made. Despite radiotherapy, the vision became more disturbed; at the present time the right eye no longer sees anything and the left only what is before it. In addition to the tumor, the patient presents an evident dwarfism (infantile dwarfism of Paltauf). In its evolution Dr. Bregman distinguishes three stages: (1) The child develops at the expense of the potential cellular energy which brings growth up to a certain stage; (2) during a second period insufficiency of the endocrine glands becomes evident, in particular of the anterior lobe of the pituitary, which in normal conditions excites the ulterior development of the cells. The consequence is arrest to a dwarf height. With time this hypofunction is expressed by still other phenomena (suppression of menstruation and disappearance of sexual appetite); (3) finally, in a third period, a tumor of the pituitary made its appearance which took on a malignant character (benign formerly; probably teratoma) and led to loss of sight.

Relations Between the Pituitary and the Testicle. — B. A. Houssay and J. M. Lascano Gonzalez (*La Semana méd.*, **36** : 1275, No. 20, May 16, 1929.)

Toads deprived of their pituitary present a very appreciable testicular atrophy at the month of operation. The testicles weigh less and there is marked atrophy of the spermatogenetic epithelium; the spermatozoids already formed persist. When only the anterior lobe is extirpated a similar atrophy is observed but less marked. In the craneotomized toads or in those with lesions in the infundibulum there is no testicular atrophy. Subcutaneous implantation of the pituitary increases the size and weight of the testicles of craneotomized toads beyond that of controls. Implantation not only impedes the atrophy in the toads deprived of pituitary but increases in size above the normal; the tubes are dilated with fluid; the activity of the spermatogenic elements is exaggerated. In some toads precocious sexual maturity is observed.

The Functions of the Pituitary and the Infundibulo-Tuberian Region in the Toad Bufo marinus (L.) Schneid.—B. A. Houssay and L. Giusti. (*La Semana méd.*, **36** : 1275, No. 20, May 16, 1929.)

The authors complete the studies on the question begun by one of them in 1910 and continued since then. The present communication is based on the observation of almost a thousand toads during the years 1927, 1928 and 1929. In this species it is possible to distinguish perfectly the symptoms corresponding to each one of the portions of the gland and to lesion of the infundibulum. The entire pituitary has been extirpated or only the glandular lobule; the tuber has been cauterized and in others only a simple craneotomy has been performed. The counterproof has been effected by means of injections of extract, grafting or repeated implantation of the distinct portions. Glandular insufficiency produces the following symptoms. Pallor of the skin by retraction of the melanophores (insufficiency of the intermediate part); tes-

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ticular atrophy; asthenia and convulsions (which certainly are not specific); high mortality; hypersensitiveness to insulin. The first symptom is very specific; the others are very intense in those deprived of pituitary, somewhat less in those deprived of the glandular lobule. These symptoms are missing in the craneotomized or those with lesions of the infundibulum. The repeated implantations, the grafting and the injections of extracts correct these symptoms. The glandular hyperfunction is revealed by darkening of the skin. The infundibular symptoms are the following. Formation of a cutaneous pellicle (trophic disturbances and ulcerations of the skin) abortion and polyuria. These symptoms are observed in toads deprived of pituitary or of glandular lobe, in the majority of those with infundibular lesions and in some with other brain lesions.

Nervous Lesions Found at Autopsy in a Subject Affected with Adiposogenital Syndrome. — L. Babonneix and J. Lhermitte. (*Rev. neurol.*, 1:495, No. 3, Mar., 1929.)

Eight years ago one of the authors presented the case of a man of 47 years in whom symptoms of four types had been noted. (1) hydrocephalus of long standing with optic atrophy, blindness and headache. (2) Hydromyelia or syringomyelia: preacher's hands, atrophy of the muscles of the hands and forearms, cervicodorsal kyphosis, abolition of tendinous reflexes to the upper members, exaggeration of the same reflexes in the lower members. (3) Adiposogenital syndrome: obesity (82 kg. for 1.58 meters height); presence of lipomatous masses in various parts of the body, testicular agenesis, gynecomastia, almost complete lack of sexual desire. (4) Polyuria.

After discussing these symptoms which appeared following repeated meningeal reactions, the first of which dated back to the sixth year, the authors conclude that it was doubtless a case of hydrocephalus with hydromyelia which had determined the production of an infundibular syndrome.

Recently the authors were able to examine the nervous system of this subject who had succumbed to a new attack of meningitis. They found very marked hydrocephalus with large dilatation of the third ventricle and atrophy of its walls, especially lower and anterior; (2) hydromyelia of the cervical marrow.

Despite the absence of all information concerning the pituitary, these observations show the importance of tuberian lesions in the production of the adiposogenital syndrome, the anatomic cause of which is still so disputed; they confirm once more the existence of an infundibular polyuria. The hydromyelia accounts for the atrophy of the upper members.

Recent Facts Concerning Hormones. — U. Ebbecke. (*Dermatol. Zeitschr.*, 55:17, 1929.)

The secretin of the intestinal mucosa which stimulates the secretion of the pancreas reaches the circulation through the hydrochloric acid of the stomach when it is excreted from the intestinal epithelium which contains it in absorption. Acetyl cholin was referred to by Le Heux as hormone of intestinal peristalsis. The sympathicomimetic adrenalin is a typical nerve hormone. Thyroid hormone increases the excitability of the vegetative nerves and in the pituitary the relation is so intimate that it is disputable up to the present which of the symptoms is to be ascribed to the pituitary itself and which to the neighboring vegetative centers of the midbrain. There is no hormone gland which does not stand in relation to the sex glands and that holds true for the endocrine glands in general. All stand in interrelationship to each other. The hormone glands are to be conceived as a complex regulating organ-function. The hormone glands influence the affective and psychic life. On the other hand the hormone glands are dependent on their secretory nerves.

Ismar Boas

(*Continued from page 83*)

excellent pedagogy and high inspiration, won the admiration and gratitude of all.

An autobiography, published in Volume VII of *Medizin der Gegenwart*, furnishes interesting and intimate details of Boas' life and at the conclusion of this article there is a comprehensive list of his writings. The individual articles amount to well over a hundred. A textbook concerning the therapy and diagnosis of diseases of the stomach has been so universally accepted that the ninth German edition has appeared. It has also been translated into English, Italian, Spanish

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and Russian. Two volumes, as a sequel to this, concern the therapy and diagnosis of diseases of the intestines, and have had two editions. The collected works of the twenty years of experience at the Boas *Privatpolyklinic* (the direction of this clinic was given over into the hands of Prof. Boas' able assistant, Dr. H. Elsner, in 1906) is published in two volumes.

Some of the special problems which have been treated by Prof. Boas are the following: Gastritis acida, occult hemorrhages, gastrogenous diarrhea, deep duodenal stenosis, enteritis membranacea, hypertrophic pylorus stenosis and its treatment, colitis ulcerosa, hemorrhoides, balneotherapeutic treatment of gastro-intestinal diseases, and other therapeutic methods. For the *Verein für innere Medizin*, in Berlin, 1900, Boas reported on the subject of carcinoma of the large intestine; for the Paris Congress in the same year, where he presided over an autopsy of the intestinal tract, he reported on enteritis membranacea. Further honors were accorded him at practically every meeting or society for the study of gastro-enterology. A report on "Chronic Appendicitis" for the Symposium on Gastro-Enterology, was published in English in the *Medical Journal and Record* (January 6, 1926). As Boas states, the report "gives not much new" but it is a careful survey of the present opinions on appendicitis, and it contains several helpful suggestions in the diagnosis of appendicitis. "Even if the diagnosis may be doubtful — of course not in typhlophobia — I am in favor of operation, particularly in children and young adults." With this statement Boas takes a definite stand on the subject of appendicitis, and for the uncertainties that still exist concerning the nature of appendicitis, he hopes that "the intelligent cooperation of surgery and internal medicine will endeavor to straighten out the difficulties." "Habitual Constipation," 1923 (translated into English by Dr. Thomas L. Stedman), has been popular, mainly for the reason stated by the author, "It is intended in no way to supplant the physician, but to second his efforts toward effecting a cure for this widespread evil through judicious counsel." The book contains sensible advice, "in non-technical terms," some unusual opinions suggestive of Coué and among other things, several special diets. In the work on diets, which was an outgrowth of the study of digestion, Boas has been both practical and thorough. It is reported that the students in his clinic were not only taught what food to prepare but also, how to prepare it, and they were required to attend classes in cooking in conjunction with their medical studies.

As a prolific scientific writer, a profound investigator, a wise counsellor and an interesting person, Boas offers a striking example of one who is not only putting a great deal into life, but is also getting a great deal out of it. He has well earned his world fame, for his work is all of the highest type and has proved universally acceptable.

The Clinical Fields of Use of the Sexual Hormone Preparations (Their Clinical Test). — R. Schröder. (*Deut. med. Wochenschr.*, **55** : 3, 1929.)

Sexual preparations well tested biologically must first pass the test of their clinical usefulness. This must be undertaken critically and also energetically if practical results are desired from the valuable theoretical biological results of this type of research. As clinical test for the hormone preparations, cases are first of all to be considered suitable in which it is a question of a moderate deficiency of ovarian hormone without other disease manifestations in the body. As clinical test analogous to the growth test in animals, there is stimulation of turgor and growth of a contracted uterus and analogous to the estrous reaction there is the time regulation of the appearance of menstruation, therefore, of the cycle tempo. On the other hand, increased menstruation or prolonged hemorrhages dependent upon abnormal processes are not suitable. These are dependent upon so many, almost always local factors of the genital tract and have not the slightest connection with the ovarian function. The use of test preparations is unnecessary in the so-called deficiency symptoms.

The question of dosage is still completely unanswered; everything is provisionally given over to the individual trial. At this time the proposal of Laqueur with his Dutch colleagues, which has just appeared in the Dutch Obstetrical Journal, is very opportune. This dosage rests on experimentation for a suitable distribution, increase of dosage and sudden cessation. It is connected throughout to the theoretical conception expounded by the author concerning the origin of the hemorrhage. Not that in any way a successful result is to be prophesied herewith, since we do not know whether the relation of sub-

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cutaneous to oral dosage is correct, or whether the absolute amount is sufficient. It is, however, possible that with this beginning we can compare the results of the different observations and make new conclusions on these bases. Patience is essential for success.

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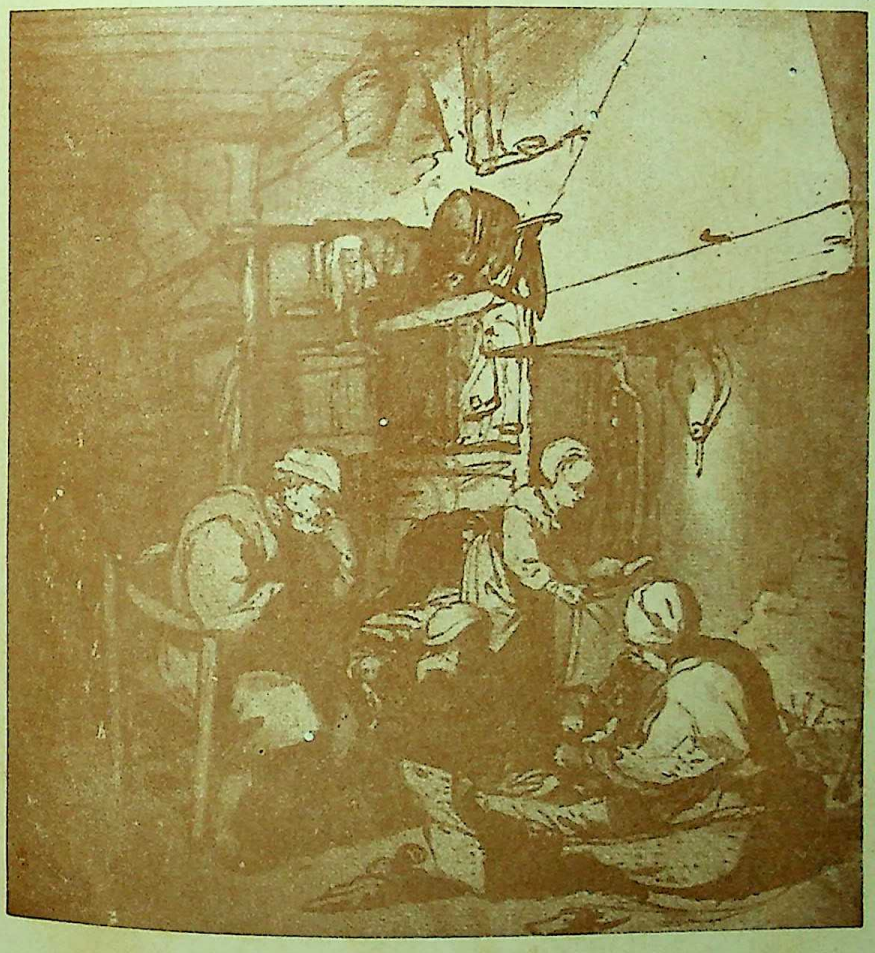
Vol. XIV MARCH-APRIL, 1930 No. 2

The Journal of Organotherapy

A Record of Progress in the Study of the Internal Secretions and Metabolism

G. W. CARNRICK CO., *Publishers*

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Abstracts · *Editorial Comment* · *Book Reviews*

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An English Physiologist's proof that Endocrine Substances supplement each other

In the *Journal of Physiology*, (Cambridge University Press, 1929, LXVIII) G. A. Clark shows experimentally that there is enhanced response to pituitary extract after thyroid feeding.

This proof is additional to a mass of evidence that is now indisputable. The endocrine substances act synergistically not only in physiology but also in therapy.

In the regulation of menstruation it is the combined effects of thyroid, pituitary, ovary and adrenals which are necessary---single gland therapy is unsuccessful therapy. It is for this reason that HORMOTONE which contains the proper proportion of potent active endocrine gland substance has proved so effective in practice in the treatment of disturbances of menstruation.



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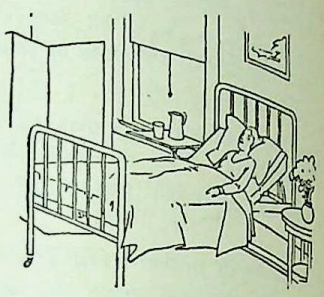
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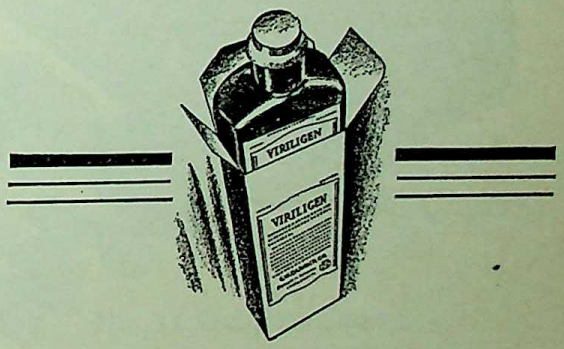
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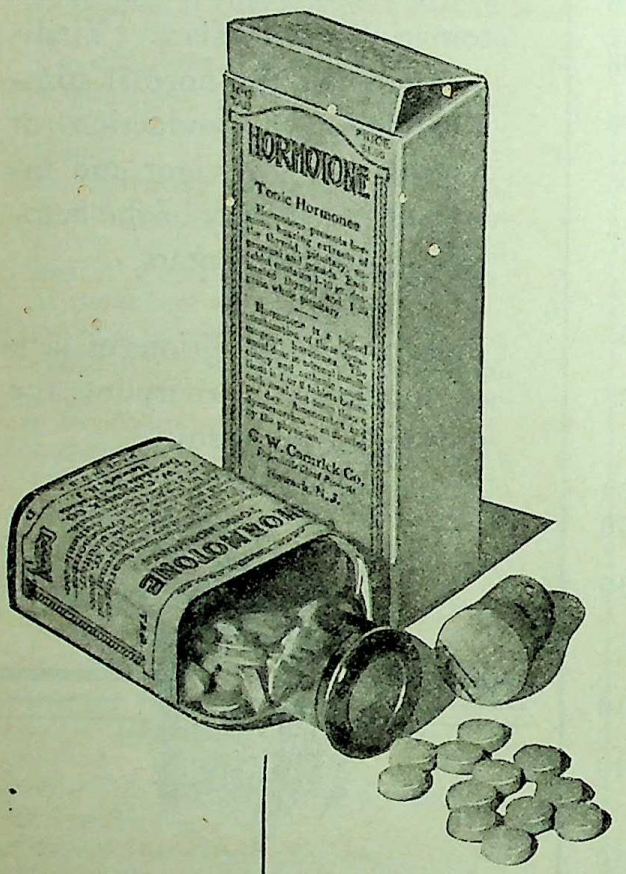
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Suprarenal grs. 1/4
Orchic grs. 1/4
Physiological Salts Comp. grs. 1/4

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Pituitary grs. 1/40
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Thyroid grs. 1/8
Suprarenal grs. 1
Ovarian grs. 1 1/2
Pineal grs. 1/30
Physiological Salts Comp. grs. 1/4

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The Journal of
Organotherapy

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Volume XIV March-April, 1930 Number 2

The "Heart Hormone" and Heart Beat

THE theory of "heart hormone" as a factor in the maintenance of the rhythm and contraction of the heart is not inconsistent with known facts of the mechanism of the heart beat. All experimental research, however, fails to give evidence of such a hypothetical hormone and, in fact, strongly negatives the theory.

THE tissues and organs of the body which may definitely be classed as endocrine and give rise to internal secretions, the physiological actions of which have been determined, is now fairly well known. It is not a large list and contains a few tissues yet in doubt. Practically every tissue of the body has been suspected of such function and has been investigated.

One of the most interesting attempts has been made to demonstrate the presence of a hormone in the heart. The changed opinion as to the cause of the rhythmic contractions of the heart muscle together with the world-wide interest in physiological endocrine mechanisms made the postulation and "isolation" of a heart hormone almost inevitable.

The description by Remak of that remarkable ganglionic mass in the sinus venosus (sino-auricular node and auriculo-ventricular node in higher animals) led at once to the hypothesis that the mechanism was a nervous one and that the rhythmic stimuli from the ganglionic node, acting as an isolated, automatic nerve center, actuated the heart muscle and gave rise to the regular heart contractions and relaxations. The researches of Gaskell and Engelmann, however, practically forced the abandonment of the theory of nerve control. In the heart of practically all animals

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rhythmic contractions may be maintained when all nerve connection to the sinus venosus is severed and even in isolated strips of heart muscle *in vitro*. The chick heart beats regularly before the development of its nerve cells.

It seemed certain from the above and other evidence of similar nature that the contracting mechanism was resident in the heart muscle cells and the stimulus to contraction might be looked for in some stimulating substance either produced in the cells themselves or brought to them through humoral channels.

The arguments for such a mechanism have more merit than mere enthusiasm for endocrine theories. The neurogenic theory seems definitely untenable. Moreover, the known facts of the mechanism of the heart beat may fairly well be reconciled with a hormone stimulation as the exciting factor. In an adult human heart the centers found in the sinus venosus of the embryo (and lower animal forms) become the *sino-auricular node* and the *auriculo-ventricular node*. From the latter arises a peculiar type of muscle tissue, the bundle of His, made up of primitive, elongated cells (the fibres of Purkinje) which form two main divisions and finally are distributed to the interior surface of the ventricles.

Since the origin of the auriculo-ventricular node lies in the upper part of the heart on the right side at the lower portion of the auricle, there is thus a direct communication between auricles and ventricles. The sino-auricular node, made up of similar tissue, also on the right auricle near the vena cava, initiates the impulses *regulating* the rhythm (but not actually causing the heart muscle contractions). Starting in the sino-auricular node this impulse extends to the auriculo-ventricular node and thus to the ventricles.

But from the standpoint of a theory of hormone control it is important to note that this sino-auricular, auriculo-ventricular mechanism is merely regulatory and that the cause of the rhythmic contractions is inherent in the heart muscle fibre. It has been noted that isolated strips (entirely separated from ner ganglia) of heart muscle may exhibit rhyth contractions for hours. The peculiar rhy mic contraction of the heart muscle fi appears to be related to the stimulus to co traction (hormone?) and the nature of the co traction itself. The work performed at ea contraction is accomplished by the utiliz tion (oxidation) of certain chemical constit ents of the cell and following contraction, t relaxation period corresponds to a period new accumulation or formation of compound constituting the "charge" for a new contrac tion. This is the "refractory" period of th heart cycle. The actual oxygen consumptio of the heart has been calculated by A. V. H (1).

"The calculated output of blood, multipli by the blood pressure, gives us the work done assuming a mechanical efficiency of 20 pe cent, which is a high value under such condi tions, the total energy used by the heart ca be calculated. The provision of this energ requires the consumption of oxygen, and would appear that the oxygen requirement the heart during such exercise as that describe above is about 300 cc. per minute—abo half its own volume. Assuming a utilisati coefficient of 75 per cent and an oxygen cap city as before, this requires two litres of bloo to pass through the coronary vessels of the heart per minute. This volume of oxyge actually used by the heart is almost equal (pe gram) to that *required* (*but not obtained*) b voluntary muscle during very violent exer cise. The muscle has to stop within a minut owing to oxygen-want; the heart, however owing to its better oxygen supply, when th coronary circulation is efficient, is able to keep up an output of this order for long periods. It would seem possible that a deciding factor in the capacity of a man for severe prolonged exercise may often be the efficiency of his coronary circulation."

Stimuli acting during the refractory period will have no effect because the conditions for contraction are not suitable. Now, if a con

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ant minimal stimulus be present, such as a hormone circulating in the fluid tissues, at each heart cycle, when the amount of contractile material is at its maximum, the stimulus of the hormone will release the energy-producing mechanism, contraction will take place and the hormone stimulus will be without effect until there has been a new accumulation of material in the cell. The question as to whether a hormone acts in some way in maintaining the constant and large oxidation in the heart as calculated above by Hill, does not seem to have been investigated.

The theory that a specific hormone is elaborated for the regulation of the heart contraction has been chiefly furthered by L. Haberlandt who, in 1924 (2), stated that he had succeeded in demonstrating a control substance formed in the sinus of the frog's heart and capable of accelerating and strengthening, on the one hand, the automatic impulse of the isolated ventricle, and on the other, of bringing the resting heart cavity to automatic activity. He referred to this stimulant substance as the "sinus hormone" and demonstrated as follows: The pulsating and bleeding sinus is plunged into a small quantity of Ringer's solution and the upper opening of the severed ventricle is at the same time connected with a cannula. This increases the strength of the pulsation and its rapidity. Ringer's solution not so passed through the heart chamber fails to give this result. With a hormone product manufactured from beef hearts, which he later calls a "heart hormone" (3) Haberlandt undertook experiments on the frog's heart. The preparation is also stated to have been clinically successful. The preparation was tested on 36 frog's heart preparations in dilutions of 1-1000, 1-500 and 1-100 with Ringer's solution. With 0.5 cc. of these dilutions the exciting, accelerating and rhythm-producing effects on the heart could be demonstrated. The pulse-exciting effect appeared in 17 experiments and the pulse-accelerating in 26, in 7 of which the automatically pulsating ventricles were first influenced chronotropically and later in the experiment the ventricle which ceased beating was stimulated to renewed action. Such results were also recorded in 7 experiments after removal of the ventricle for a period of 1 day and in 3 experiments after 2 days removal. It was also shown that the "heart hormone" in dilutions of 1-1000 sensitizes the frog's heart ventricle to adrenalin, similar to the effect observed by Demoor and Rijlandt, of aqueous extracts of sinus node on the auricles of warm-blooded animals.

Haberlandt's experiments, despite the fact of the relatively low percentage of positive results (not much more than 50 per cent) and lack of controls, were highly stimulating. Haberlandt's work did not show that the stimulating substance was specific, *i.e.*, whether it was exclusively elaborated in the heart. Subsequent investigations seem to clearly negative this. Rigler and Singer (4) undertook to repeat the experiments of Haberlandt, following the identical procedure under the general direction of Professor Rothberger. They succeeded in demonstrating a stimulating action on the isolated heart, but their positive results as compared with negative were more unfavorable than Haberlandt's. They demonstrated, moreover, that ventricular substance itself (not sino or auriculo node) produced a stimulating substance active in the frog heart apices. They concluded that the stimulating substance is not formed in a specific tissue but in various, widely differing tissues and sites of the body — lower portion of heart ventricle, lungs, liver, spleen and testicles all gave aqueous and alcoholic extracts containing a stimulating substance which can not be distinguished from Haberlandt's, either in its inotropic (affecting the force or energy) or chronotropic action (affecting the rhythm) on the heart or in its solubility or heat stability. Similar substances have also been extracted from the skin (5) and the liver (Asher). Asher (6) in a review of his own work and that of his pupils inclines to the

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opinion that the active constituents of his liver extracts which stimulate the heart are due to cholates. In high dilutions they increase the strength of the heart (inotropic action) and slow the pulse (chronotropic action). In lower concentrations they increase both the strength and the frequency. These results are interesting when we consider the preparation "Eutonin" the "heart hormone" prepared from the liver by G. Zuelzer.

E. D. Oppenheimer (7) also investigated the specificity of this heart stimulating substance. The following tissues were investigated — sino-auricular node, right and left auricles, right and left auricular appendages, right ventricular wall and the base and apex of the left ventricle. Control experiments with tissues other than the heart were made, using striped muscle from the thigh, diaphragm and upper end of the esophagus; smooth muscle from the intestine, stomach and lower end of esophagus, liver, lung and brain. The extracts were made as follows:

"The tissues were obtained from the animal as soon as possible after death, and a weighed amount was ground thoroughly to pulp with a small quantity of Locke's fluid and clean sea-sand. After trituration, the paste was diluted further in the proportion of 1 gram of tissue to 15 cc. (or in later experiments, 10 cc.) of Locke's solution. The mixture was allowed to extract for several hours (generally overnight, for about 18 hours) in a refrigerator, was then centrifuged, and two or more cubic centimeters of the clear fluid used for injection.

"In some cases an alternative extraction was made in a similar way with 95 per cent alcohol. The alcoholic mixture was extracted for 18 hours in a corked flask, was centrifugalized, and the supernatant fluid allowed to evaporate to dryness at room temperature. The residue was then extracted with a quantity of Locke's solution equal in amount to the original alcoholic extract.

"The extracts were warmed exactly to the temperature of the perfusing solution before injection, and were injected slowly so as [illegible] cause no rise of pressure in the aorta or [illegible] onary system."

Oppenheimer is in general accord with [illegible] work of Rigler and Singer (above).

"These results show without doubt [illegible] there is frequently present in extracts of hea[rt] muscle a substance which has a stimulati[ng] action upon the beat of the isolated hea[rt] causing augmentation and often accelerati[on] of the beat, and sometimes initiating a be[at] in a previously quiescent heart, but oft[en] followed by a toxic action.

"The nature of this substance, however, appears less certain, as does also the questi[on] of its specificity and origin. According [to] Haberlandt (1927) it should be regarded as [a] true hormone, which is produced in the sin[o-] auricular node and other parts of the 'spec[ial] musculature' of the heart, and has the specif[ic] function of initiating and controlling the hea[rt] beat. This viewpoint has been recen[tly] challenged by many other writers (Rigler an[d] Singer, 1927; Rigler and Tieman, 19[27]; Rigler, 1928; Weichardt, 1927; Kisch, 192[7]) and the present research suggests that th[ese] doubts are well founded. There is no e[vi]dence that an extract of sino-auricular n[ode] is more active than that of other regions [of] the heart; in fact, an extract of the auric[le] (either right or left) usually has a rather more strongly augmenting action than that of th[e] sino-auricular node. Other parts of the hea[rt] also, are in many cases equally active, and [the] apex of the ventricle, completely free fr[om] endocardium to exclude the specialized co[n]ducting (Purkinje) cells, may have just [as] strong an augmenting action as the base.

"In fact, in most experiments the effects [of] extracts of different parts of the heart [are] quite indistinguishable. No support, therefore, is obtained from the view that [the] stimulating substance is manufactured only in the special musculature, attractive though such a theory undoubtedly is. . . ."

"Taking all these facts into consideration it seems doubtful whether one is justified

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garding this augmentor substance as a pecific hormone, whose function is to initiate and control the heart beat. The fact seems rather to suggest the presence of some product of metabolism in these tissue extracts. Weichardt (1927), indeed, has put forward the view that Haberlandt's 'heart hormone' is merely a particular example of his general hypothesis of the 'function-increasing' action of cleavage products. . . ."

"It appears certain, therefore, that not only is this heart stimulating substance of somewhat inconstant action, and present in only small amounts, but that the special musculature of the heart is by no means the only tissue where it may be found. Whether ultimately it will prove identical with histamine or not, at present the evidence of its specificity as a heart hormone is extremely doubtful."

The evidence of the existence of a heart hormone, arising in a specific tissue and exerting specific effects is incomplete and unconvincing. Heart stimulating substance or substances are found not only in the nodes of the heart but in the heart muscle in which there is no question as to the absence of any specialized tissue. Moreover, these substances may be found in various tissues bearing no type relation to each other. Rigler and his associates have suggested that these substances occur as normal products of body metabolism and exercise this hitherto unsuspected function. They have shown that the substances exert effects similar to histamin on uterine muscle and on blood pressure. Numerous observers have suggested the similarity to histamin in both its pharmacological effects and chemical characteristics. The point of action in the heart mechanism is not clear. Rigler believes that it acts on the anaerobic phase of heart muscle metabolism since the contraction, exciting and strengthening effects may be demonstrated on isolated Purkinje fibres which are believed not to require oxygen in their metabolism. The toxic effects characterizing so many experiments do not inspire confidence in these preparations as containing a true heart hormone. At the present time not only will entirely new evidence have to be submitted but a mass of existing evidence will have to be disproved.

1. Hill, A. V., Muscular Activity, Lectures on the Herter Foundation, Johns Hopkins Medical School, 1924.
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3. Haberlandt, L., *Med. Klin.*, 1928, xxiv, 22.
4. Rigler, R., and Singer, R., *Klin. Wochenschr.*, 1927, vi, 2357.
5. Weichardt, W., *Klin. Wochenschr.*, 1927, vi, 1555.
6. Asher, *Schweiz. med. Wochenschr.*, 1926, lvi, 1921.
7. Oppenheimer, E. D., *Am. J. Physiol.*, 1929, xc, 656, Nov. 1.

A Contribution to Kottmann's Reaction

(Translated from the article by Dr. Emil Walder, *Mitt. Grenzgeb. Med. u. Chir.*, 1926, 39 : 626, No. 4/5.)

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(CONTINUED FROM VOL. XIV, No. 1)

II. *Clinical Results*

As regards our clinical results with the Kottmann reaction, we may once more stress that the figures noted on our accounts of experiments are no other than degree of browning, which were determined with the as-

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sistance of the standard. In our tables AVBS signifies blood serum from the arm vein and KVBS signifies goiter venous blood serum.

Whether conclusions may be drawn from the greatness of the discrepancy between degree of browning of the arm and goiter venous blood serum concerning the functional state of the thyroid we wish for the time being to leave undecided. We wish merely to note here that in general the goiter venous blood serum shows less marked browning; begins with a lesser degree of browning and shows a slower course of browning, as well in ordinary goiters (as may be observed from the following tables), in cretins (here perhaps most markedly) as in exophthalmic goiter, where we might properly expect theoretically that the difference would be greatest in exophthalmic goiter (reaction error?). A reverse behavior, accordingly, more marked browning of the goiter venous blood serum than of the venous blood serum from the arm we never observed.

Table 1. Degree of Browning of Normal Sera

Venous Blood Serum from the Arm (AVBS)

Minutes after Addition of Hydrochinon	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
0	7	8–9	7–8	7–8	9	8	6
5	7	11	7–8	8	9	10	6–7
10	7–8	11–12	8	9–10	9–10	10	7
15	9	11–12	9	10–11	9–10	11	8
20	9–10	11–12	9–10	10–11	9–10	11	9
25	10	11–12	10	10–11	9–10	12	9
30	10	11–12	10	10–11	9–10	12	9

Table 2. Degree of Browning of Ordinary Goiters

Minutes after Addition of Hydrochinon	Case 1, G. M., 31 yrs. Str. nod. parench. + coll. Pregnancy in 2nd month		Case 2, K. W., 15 yrs. Str. nod. microfoll. and tubul. Basal Metabolism + 5% Rat +		Case 3, W. F., 20 yrs. Str. diff. coll. Basal Metabolism + 20% with marked stenosis. Rat 0	
	AVBS	KVBS	AVBS	KVBS	AVBS	KVBS
0	....	....	....	....	....	....
5	8	5–6	6	5–6	5	3–4
10	9	8	11	8	7	5–6
15	9–10	9	11–12	9–10	8	7
20	9–10	9	11–12	10–11	9	8
25	9–10	9	12	11	10	9
30	9–10	9	12	11	10	9

If we consider Table 1, Degree of Browning of Normal Sera, 7 cases, we see that the reaction in these begins with a degree of browning of 7 or 8 and ends with 10 or 11 or 12 (Case 1, 3, 4 and 6). There are also to be sure deviations from this behavior (case 2, 5 and 7). We leave it undecided whether these three cases are dependent upon errors in the method or faulty choice of the normal sera or both together — as much as possible individuals were chosen who were goiter-free, intellectually, psychically and physically normal. Standard 12 appears to be the upper standard 10 the lower limit for a maximum developed normal serum. Case 7 resembles a mild exophthalmic goiter very much, beginning with 6+ and ends with 9+, turning brown very slowly.

Cases 2 and 6 appear to stand at the upper limit of the normal sera, where the hyperthyroidism soon begins.

Table 2 shows the results in 3 ordinary

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goiters. Among ordinary goiters we understand the cases without clinical symptoms of hypo- or hyperthyroidism, hence physically, psychically and intellectually normal individuals, who are afflicted with a more or less large goiter (condition of euthyroidism).

Case 1 resembles with regard to the Kottmann reaction, a normal serum, perhaps standing on the border towards exophthalmic goiter. Pregnancy in the second month was, however, present; what influence pregnancy has on the result of the Kottmann reaction in the serum, whether direct or via the thyroid, we do not know. It is conceivable that a pregnancy serum assumes exophthalmic goiter like characters as far as the Kottmann reaction is concerned. The goiter venous blood serum distinctly follows after the venous blood serum of the arm in becoming brown as also in the two other cases.

Case 2 is normal according to basal metabolism and rat test. According to Kottmann's reaction the serum resembles a normal serum which stands on the border towards hypothyroidism. The reaction begins to be sure with the low standard degree 6, rises immediately, however, to 11.

Case 3 has a basal metabolism of +20 per cent, probably owing to the marked stenosis of the trachea; no clinical symptoms of hyperthyroidism. Rat test equals 0. Here the Kottmann reaction resembles that of a normal serum, only the reaction begins with a somewhat low degree of browning.

Table 3. Degree of Browning of Exophthalmic Goiter Sera

Minutes Following Addition of Hydrochinon	Case 1. S. A., 40 yrs. Clinically: Basedow. Str. nod. parench. + diff. coll. (Basedowiana). Basal Metabolism + 39.31%. Following ligation of Both Superiores, Basal Metabolism + 9.17%. Rat 0 to +		Case 2. K. O., 31 yrs. Iodin Basedow (Sajodin). Basal Metab. + 47%. Rat ++. Lymphocytosis, 36%	Case 3. L. F., 27 yrs. Pregnancy in 5th Month. Clinically: Hyper- + Hypo-symptoms. Basal Metabolism −1.4%. Rat +. Lymphocytosis 28%	
	AVBS	KVBS	AVBS	AVBS	KVBS
0	5	6	1–2	....	....
5	5–6	6–7	3–4	3–4	2–3
10	5–6	6–7	6	7–8	6–7
15	7	6–7	6–7	8–9	8
20	7–8	6–7	7–8	9	8–9
25	8	6–7	7–8	9+	9−
30	8–9	6–7	7–8	9–10	9−
Minutes Following Addition of Hydrochinon	Case 4. K. C., 25 yrs. Clin. Basedow. Str. diff. parench. (Based.) + Thymus persist. Basal Metabl. + 14.77% +++ Lymphocytosis 48%. 2 Months after Operation: Basal Metab. −6.53%. Rat 0. Significant Subjective Improvement		Case 5. K. Clin. Basedow. Rat +	Case 6. B. F., 12 yrs. Iodin Basedow? Basal Metab. −1.35% or −12.43%. Rat: AVBS + KVBS +	
	AVBS		AVBS	AVBS	KVBS
0	....		6	4–5	4
5	6–7		6	9+	8+
10	7–8		6–7	9–10	9
15	8		7	9–10	9+
20	8–9		7–8	10−	9+
25	8–9		8−	10−	9+
30	8–9		8−	10−	9+
45	9		8−		....

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The degree of browning of exophthalmic goiter sera (6 cases) shows the following relations:

Case 1 concerns a 40 year old patient with Struma nodosa parenchymatosa + diffusa colloides (Basedowiana). Lymphocytosis 41 per cent; basal metabolism +26.87 per cent on the 20th of April, 1923; on the 1st of June, 1923, basal metabolism + 39.31 per cent; on the 2nd of June, ligature of both Aa. thyr. sup.; 2 weeks later on June 15th, basal metabolism +9.17 per cent and rat test with rat reaction to venous blood serum from the arm 0 to +. On August 14th, resection of the goiter and ligation of the Aa. thyr. inf. on both sides. Then, removal of blood for the Kottmann reaction. The browning of the arm venous blood serum corresponds to a moderate to medium degree of exophthalmic goiter, with which gas exchange and rat test harmonize pretty well; the goiter venous blood serum at the beginning of the reaction is about 1 standard degree browner than the arm venous blood serum (reaction error?). The browning increases, however, only about ½ standard degree, so that the arm venous blood serum at the end of the reaction is about 2 standard degrees browner than the goiter venous blood serum.

Case 2 is an iodin Basedow (preliminary treatment with Sajodin) with a basal metabolism of + 47 per cent, rat + +, lymphocytosis 36 per cent. The Kottmann reaction of the venous blood serum from the arm agrees well with this finding and with the clinical picture; begins with 1-2, turns brown relatively slowly and terminates with 7-8.

Case 3 is clinically a mixed case: hypo- + hyper-symptoms in addition to pregnancy in the 5th month. Basal metabolism — 1.4 per cent. Rat +. Lymphocytosis 28 per cent. The browning of the serum is such that one can not decide whether it is a question of a very slight degree of exophthalmic goiter or the influence of pregnancy.

Case 4. Twenty-five year old female patient with clinically distinct exophthalmic goiter, Struma diffusa parenchymatosa (Base-dowiana) + thymus persistence. Basal metabolism + 14.77 per cent, rat test +. Lymphocytosis 48 per cent. Two months after the operation gas exchange −6.53. Rat 0. Subjectively, distinct improvement. In this the venous blood from the arm shows slight degree of exophthalmic goiter according to Kottmann.

Case 5. Distinct exophthalmic goiter. Rat +. Venous blood from the arm according to Kottmann shows medium degree of exophthalmic goiter.

Case 6. Thirteen year old boy with questionable iodin exophthalmic goiter. The basal metabolism (−1.35 per cent and −12.5 per cent at a second determination) speaks against it. The rat test: venous blood serum from the arm +; goiter venous blood serum − likewise speaks against this diagnosis. In the beginning, Kottmann's reaction resembles that of exophthalmic goiter (accident?), remaining course and end reaction behave like normal serum.

It is therefore a question of four clinically sure but mild cases of exophthalmic goiter and of two cases whose clinical diagnosis was at least doubtful, and which were not hyperthyroid even after basal metabolism and rat test. The exophthalmic goiter cases showed 2 to 3 scale units less browning than the normal cases; these border cases on the other hand behaved like the latter.

The degree of browning of 6 cretin sera showed the following relations:

Cases 1 and 2 concern two sisters, pronounced dwarf cretins with Struma nodosa parenchymatosa + atrophy of the thyroid lobe.

Gas exchange. 22.8 per cent or 26.64 per cent
Rat — or —

The Kottmann reaction in venous blood serum from the arm agrees with this. The reaction begins with 10 browning degrees, increases rapidly and after 30 or 25 minutes the browning is more marked than 15. The

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Table 4. Degree of Browning of Cretin Sera

Minutes after Addition of Hydrochinon	Case 1. B. R., 43 yrs. Dwarf cretin with Str. nod. parench. + Atrophy of the thyroid lobules. Basal Metabl. −22.8%. Rat − −	Case 2. B. E., 48 yrs. Struma nod. Dwarf cretin Gas Exchange − 26.64%. Rat −	Case 3. O. A., 14 yrs. Cretin. Struma nod. parench. lymphocytes 29%	
	AVBS	AVBS	AVBS	KVBS
0	10	10	4–5	4–5
5	11–12	12	6–7	5
10	13	13–14	8–9	6–7
15	13+	14–15	11	9–10
20	14–15	15	11–12	10–11
25	15	More than 15	12	11
30	More than 15	More than 15	13	11–12
45	More than 15	More than 15	13–14	11–12

Minutes after Addition of Hydrochinon	Case 4. J. F., 24 yrs. Cretinoid. Struma nod. parench. microfoll.		Case 5. N. E., 14 yrs. Str. nod. parench. Clin. Cretinism. Lymphocytosis 35.5%. Basal Metab. −5%		Case 6. H. C., 27 yrs. Clin. Distinct Hypo. Basal Metabl. + 7.87% Rat. 0. Str. nod. parench. cyst.	
	AVBS	KVBS	KVBS	KVBS	AVBS	KVBS
0	.....	.....	4	3–4	7–8	7+
5	13	6–7	4–5	3–4	8	7–8
10	13	8	4–5	4	9+	8+
15	13–14	9	5	4–5	9–10	9
20	13–14	10+	7	6–7	10−	9+
25	13–14	10–11	8–9	8–9	10−	9–10
30	13–14	10–11	9+	9	10−	9–10
45	.....	.....	9+	9	10−	9–10

are the most marked degrees of browning which we have ever obtained.

Case 3, clinically youthful cretinism looks like hypothyroidism in the Kottmann reaction also, only the reaction with arm as well as goiter venous blood serum begins with standard 4 to 5 (reaction error?).

In Case 4, mild goitrous cretinism, the serum developed according to Kottmann reaction is again distinctly hypothyroid.

In Case 5 the result of the Kottmann reaction does not absolutely agree with the clinical picture (pronounced cretinism, basal metabolism − 5 per cent, lymphocytosis 35 per cent), since according to Kottmann we would sooner conclude a mild degree of exophthalmic goiter and clinically no symptoms of hyperthyroidism were to be found.

Case 6 is a border case, clinically definite hypothyroid, basal metabolism +7.87 per cent. Rat 0. The Kottmann reaction behaves like a normal serum.

(To be concluded)

Practical Therapeutics

Thyroid Therapy

THE use of thyroid in medicine is based fundamentally upon its remarkable action in increasing the metabolism of body cells. There is no known substance that will exert a comparable stimulus to cell metabolism and it is this definite pharmacologic action that makes it such a valuable

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therapeutic agent. The action is probably catalytic and resembles that of epinephrin, although much more active.

"The physiological action of thyroxine and of epinephrine appear to depend in large part on their effect on processes of oxidation in the animal organism. The weight of material suggests that they act as catalysts. Studies in respiratory metabolism and in oxidation in vitro have afforded an approach to this problem which has already resulted in significant progress." (Kendall-"Thyroxine," 1929.)

The action of thyroid is not specific for any particular type of cell or tissue. Of the several foodstuffs protein fats and carbohydrates all show accelerated oxidation following the administration of thyroid. "The conclusion can be safely drawn that the primary reaction, which is altered by a change in the concentration of thyroxine in the tissues, is intimately associated with an increase in the consumption of oxygen and the output of carbon dioxide" (Kendall).

This non-specific action on cells of all types explains the diversity of therapeutic uses. The article of Oswald (abstracted below) enumerates most of them. In the host of symptoms due to a definite lack of thyroid secretion thyroid gives rise to results little short of astonishing. In infants lack of thyroid hormone gives conditions ranging from a few symptoms referable to the skin and its appendages and slight mental "backwardness" to the marked structural defects, dwarfism and idiocy of fully developed cretinism. It is a question of the degree of the thyroid deficiency, the age and the constitutional type of the patient. In all but the most profound types of mental involvement and in those which have continued for years without treatment, thyroid practically effects a restitution to normal. Even in the marked effect of thyroid on growth there does not seem to be a question of specific effect:—apparently the lack of stimulation to the metabolism of the epiphyses and other growth factors is sufficient to explain the action.

In obesity of various types but particularly endogenous obesity it is usually believed to be effective by reason of its stimulation of greater oxidation of nutritive matter. This probably the explanation although indirectly it may be related to the storage of foods as glycogen. Thyroid administration lowers the glycogen content of the liver. Hypothyroidism is attended by the same condition. Thyroid stimulates the glycogenic function of the liver and the oxidation of glucose by the cells. It is of undoubted value in several types of obesity, but requires as much care and experience on the part of the physician as the administration of insulin. Oswald's observation that it acts through a dehydrating effect on the organism does not seem particularly convincing. Certainly the effects of thyroid reduction of weight are not comparable to the results of drugs exerting a purely dehydrating effect.

Of greatest interest to general medicine however, is the effect of thyroid in raising metabolism in that class of patients who exhibit generally lowered vitality and lack of energy. The action of thyroid in increasing oxidations and liberation of energy together with its action in increasing the activity of the autonomic nervous system make it a therapeutic agent of unusual value. The autonomic nervous system, through its function of maintaining "tone" of the visceral unstriped muscle fibre, is an excellent way of approaching to increasing the "vitality" of the tissues.

A practical point to be considered in thyroid therapy is the delayed action characteristic of this substance. From 6 to 10 days are required to give the maximum effect on basal metabolism. This applies either to injection of pure substance, thyroxin or to the oral administration of desiccated thyroid.

The possibilities of thyroid in therapy have not as yet been realized.

Thyroid Therapy, Its Indications and Contraindications.—A. Oswald. (*Klin. Wochenschr.*, 1926, 5 : 1618.)

In addition to deficiency of the thyroid gland (the complete abolition of its functio

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there is an insufficiency (a simple decrease of it). On this basis arise the incomplete, partial or mitigated forms of myxedema. In this condition, not infrequently one single symptom surpasses all others and appears especially to be the only abnormal symptom. Indeed, occasionally chronic constipation stands entirely in the foreground and many a case of chronic functional constipation is merely the expression of an hypothyroidism and reacts in a striking manner to thyroid therapy. In other cases, obesity stands in the foreground of the disease picture (thyrogenous obesity). Dietetic treatment is wholly without effect, while thyroid therapy often has an astonishing action. This type of obesity is encountered as well in adults as in children. The pasty, chlorotic, obese types also belong here.

In other cases, the hypothyroidism asserts itself in the form of chronic metrorrhagia with every objectively visible finding lacking in the genital apparatus. Neither the use of styptic remedies nor repeated curetting has results, but thyroid therapy helps in a striking manner. Many cases of pregnancy nephrosis and an edematous tendency of the tissues often appearing in pregnancy are indeed to be conceived of as the expression of hypothyroidism. Here, there appears to be a secondary involvement of the thyroid on the basis of an ovarian insufficiency. In these cases also, does thyroid therapy have a favorable effect. The same would apply for climacteric edema.

Not infrequently manifestations of chronic rheumatism rest upon masked hypothyroidism. That this conception is justified, aside from the therapeutic effect, is shown by the fact that Kocher's "thyreoprivic equivalent" of this type is not infrequently observed following strumectomy. Such cases react especially well to thyroid therapy, defying all other therapy.

At other times, ulcerous dermatitis, among other things in association with localized edema or corpulency, acne, furunculosis, or chronic eczema, is the expression of a hypothyroidism. These cases defy the usual dermatologic methods of treatment, but heal promptly and completely with thyroid administration.

With the above mentioned indications the field of thyroid therapy is not exhausted. Thyroid therapy may be used quite suitably in all cases where one wishes to raise the metabolism and general vital energy. This effect is to be traced back to the beneficial effect proved by experiment, on the oxidation processes and the tonus-increasing action in relation to the visceral nervous system. Thus, Oswald employed thyroid treatment successfully in anemic, asthenic conditions, provided no nervous element was present; in avitaminosis (beriberi), the trophic disturbances are favorably influenced, perhaps through elevation of sympathetic hypotonia. Thyroid medication has also been used effectively to assist callus formation of fractures. This action finds experimental support in the fact that callus formation in the thyroidectomized animal is demonstrably retarded and may be normalized by the administration of thyroid substance. On the other hand, the interesting observation was made that in fractures with the appearance of osteoid tissue in the callus, signs of increased thyroid activity appear in the histological picture of the gland. The application of thyroid preparations supports this action.

Thyroid medication has occasionally a good effect in retarded development which is not of hypothyroid nature, in universal dystrophic infantilism. Also for this effect, must we call upon the metabolism and growth stimulating properties of the thyroid hormone.

Thyroid therapy is a very valuable aid in the treatment of obesity, including obesity of non-thyrogenous origin. Through its well known diuretic property, it serves to dehydrate the organism and at the same time through its property of furthering oxidation, it increases oxidative processes. Self-evident in such cases is the exhortation for caution and for continuous control of the heart.

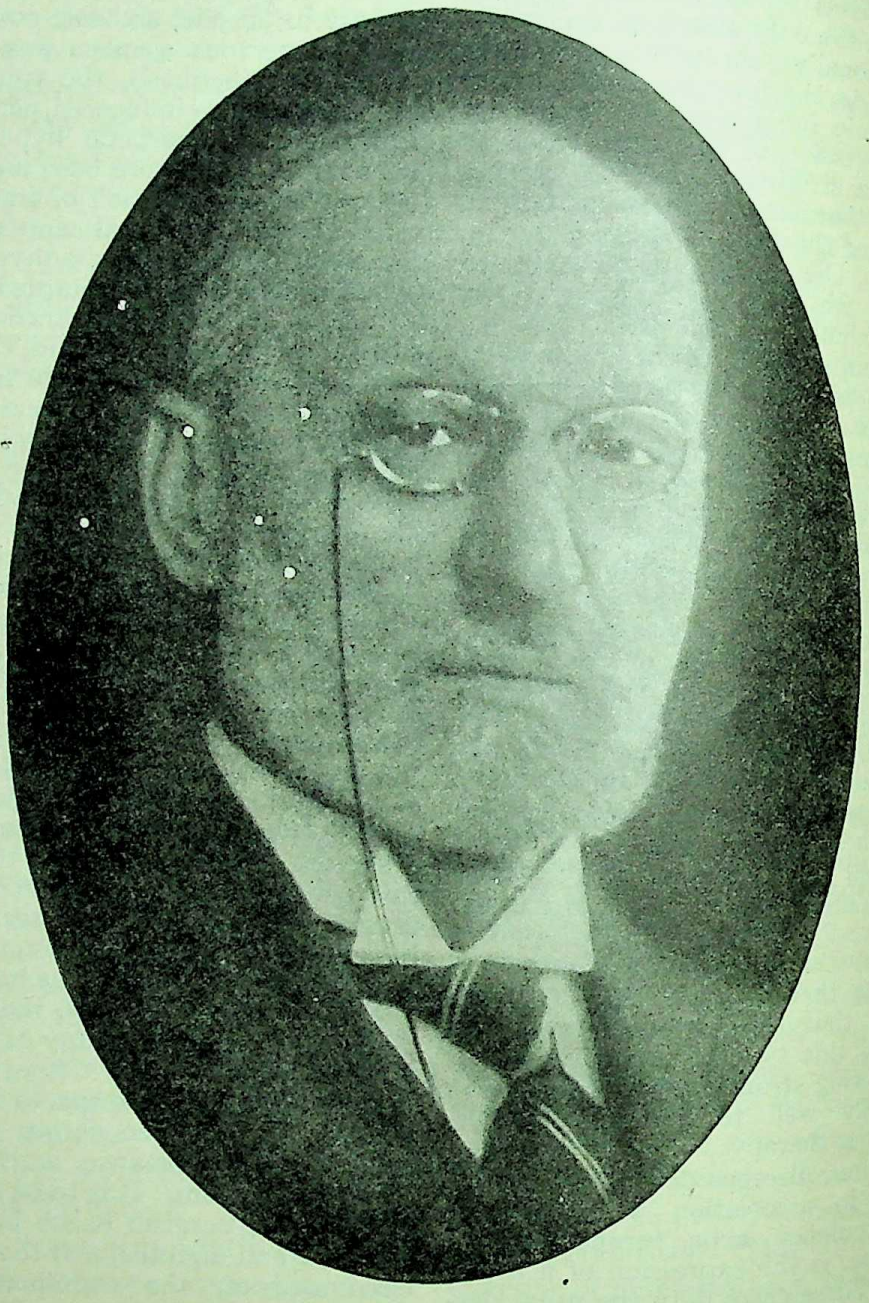
Thyroid therapy is also indicated in genuine nephrosis and in many extrarenally conditioned edemas. The tissues themselves or the intercellular tissue spaces are its point of attack. It has been shown experimentally that thyroid substance activates salt and water metabolism. It is to be mentioned that a positive synergism exists between thyroid hormone and digitalis, and that under certain circumstances, the combination with this medication is to be recommended (Eppinger, Mautner). It appears as if the thyroid hormone strengthens the diuretic effect of digitalis. There are cases in which digitalis fails, where, however, good diuresis occurs, when simultaneous small doses of thyroid preparations are given.

(*Concluded on page 108*)

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The Doctor's Page



ISMAR BOAS

(1858-)

For some scientific workers the name of Ismar Boas may be associated with specialization of gastro-enterology and the founding of the first clinic for the treatment of gastro-intestinal diseases as a separate phase of internal diseases. Others may recall him in connection with an abundance of excellent scientific literature, both in periodical and book form, concerning numerous problems in the gastro-intestinal system: digestion, constipa-

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tion, gastric ulcers, gastritis, determination of lactic and hydrochloric acid in the stomach contents, methods of exploring the stomach and its contents. His name is also associated with that of Oppler in the discovery and nomenclature of the lactic acid fermentation bacillus and with several instruments for use in the diagnosis and therapy of gastro-intestinal diseases. Boas' reagent tests for hydrochloric acid and for lactic acid in the stomach are well known. In short, the quantity and quality of Boas' scientific endeavors substantiate the wisdom of his decision to segregate gastro-intestinal from the study of other internal diseases.

Boas' life began in Exin, in Posen, in the western portion of Poland, March 28, 1858, in the large family of a small merchant. The first years of his life were pleasant, for this family was gifted with happy dispositions. The parents wished to give their children a good education, but, unfortunately, the family finances were not abundant, so that it sometimes became a serious problem to pay both the baker and the tutor. However, persistency and a youthful heart helped Boas to face these difficulties valiantly, and meanwhile, to make the most of the little pleasures he was able to obtain while he stored away hard earned knowledge which was to bear ample fruit at some future date.

Boas was sent, with an older brother, to a neighboring *Gymnasium* at Nakel, and then to Züllichau, for preliminary education. In 1877 Boas began the study of Medicine at Berlin, continued it at Halle and completed it at Leipzig where, in 1881, he received the doctorate in Medicine. The dissertation for this occasion concerned the subject of paroxysmal hemoglobinuria, published in *Archiv für klinische Medizin*. It is commended as an excellent clinical study.

Boas was attracted by the experiments, on animals, of C. E. Ewald, Frerich's assistant in Berlin. At the opening of the course of lectures which Ewald was delivering on the subject of physiology of digestion, there were five students enrolled. One by one these dropped out of the class until, at the conclusion, Boas was the sole, faithful survivor. This work was one of the first stimuli to Boas' scientific career, for he was not only interested in the theoretical knowledge obtainable, but he also acted as an experimental subject, himself.

Boas traveled for about a year after graduation, and when he found he was able to do so, he established himself in practice in the environs of Berlin (1882). Then he renewed his former brief association with Ewald, served him as private secretary and assisted in the publication of the *Berliner klinischer Wochenschrift*, of which Ewald took charge at the death of Waldenberg. Later Boas became Ewald's assistant in the Women's Hospital. Here the scientific problems which were ultimately to bring him world fame began to assume proportions. The fundamental experiences for the methods of chemical analysis of the stomach and the succussion experiments were first done at this laboratory. The results of the pathological and physiological findings concerning the digestive system were published in *Virchow's Archiv* (Volume 101, 1885) and in the next year Ewald and Boas contributed further on the same subject (Volume 104, 1886), concerning the lowering of the HCl curve after doses of oil, destruction of ptyalin after high degrees of HCl and the amylolytic and proteolytic stages of gastric digestion.

During the study of literature dealing with the stomach and intestines for this portion of his work, the idea occurred to Boas that this phase of internal diseases was so vast that it might well be segregated for special study, from the rest. He thoroughly convinced himself of the efficacy of this action and then set about establishing himself as a specialist in diseases of the gastro-intestinal tract. Intense disagreement ensued with Ewald, which was never to be entirely bridged over again. Boas' point of view, in the face of the current objections, is well explained in the preface to "Diseases of the Stomach" (1907, translated from the 5th German edition). "Just as the diseases of the nervous system have emancipated themselves from the maternal trunk of internal medicine, without having given up the connection with it, the pathology of diseases of the digestive organs must — if it shall maintain its estate — not by any means lose the connection with the general practice of medicine."

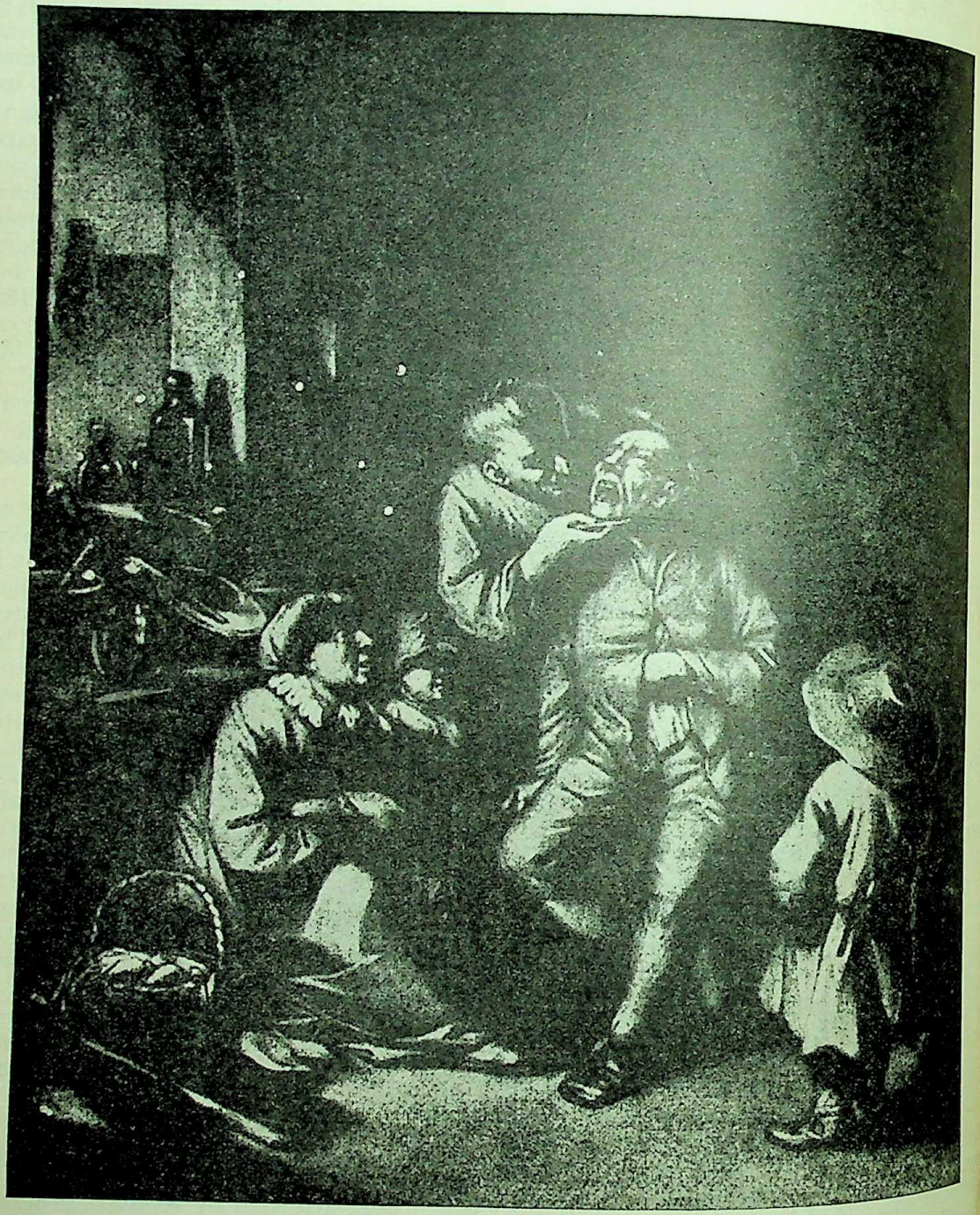
Intent on his own beliefs and disregarding the adverse opinions, Boas founded his clinic for this special study, he gave courses in it which were attended by scores of students of other countries as well as of Germany, and he gave capable young physicians, who attended his classes, opportunities to serve as his assistants. He offered wise counsel; and, with

(*Continued on page 122*)

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Medical Subjects by Famous Masters



"EXAMINING THE MOUTH AND THROAT," by Cornelis Pietersz. Bega (1620-1677)

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Editorial Comment

The Journal of Organotherapy

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Insulin in Non-Diabetic Cases

THE JOURNAL has frequently commented upon the several uses of insulin in cases other than diabetes. Malnutrition, vomiting in infants, in pregnancy and eclampsia, have all been more or less successfully treated with insulin. Schiff (abstract below) discusses the use in ketonemic vomiting in children. He can see no basis for the treatment principally because there is no incontrovertible evidence of an insulin deficiency in children displaying ketonemia and vomiting.

That particular form of acidosis, ketosis or ketonemia, is not only common in diabetes but in childhood as well, and in cyclic vomiting in children there is frequently found large production of keto-acids. There is also a consequent lowering of the alkaline (bicarbonate) reserve. This type of acidosis is usually due to imperfect oxidation of fats — the fatty acids undergoing oxidation until a 4 carbon acid is reached and future oxidation fails at that point. The result is an accumulation of the ketone bodies (beta-oxybutyric acid, diacetic acid and acetone) and an acidosis.

These disturbances in fat metabolism seem to occur in apparently healthy children. There is no question of diabetes or hypoinsulinism present; it is an as yet unexplained phenomenon. It is known, however, that the imperfect oxidation of the fatty acids is almost always accompanied by an imperfect oxidation of carbohydrates. Fats burn in the fire of carbohydrates. Now insulin aids in the oxidation of carbohydrate (sugar) in both diabetic and non-diabetic organisms. It, of course, has other functions, none of which is entirely understood. In the case of accumulation of keto-acids, however, in the blood, the administration of sugar and the concurrent injection of insulin would seem to have a theoretical basis of use by providing an increased burning of sugar which acts as a necessary condition for complete oxidation of the fatty acids. Marriott and Hartman have shown that in the treatment of this type of acidosis in diabetes, the administration of insulin and water is usually sufficient by completely oxidizing the keto-acids and thereby releasing the combined base. This in part restores the lowered alkali of the blood. They found that the concurrent administration of sugar can aid in increasing the keto-acid oxidation and that in great degrees of alkali lowering in the plasma, administration of alkali is effective. Schiff's observation, therefore, that the combined use of sugar and insulin in ketonic vomiting is superfluous, does not seem to be entirely acceptable in the absence of specific proof on this point.

Ketonemic Vomiting and Insulin Therapy. — E. Schiff (*Monatschr. f. Kinderhlkde.*, **42** : 429, 1929).

Favorable therapeutic results were reported by various authors in ketonemic vomiting of children. Without doubt ketonuria in analogy to diabetic coma gave the stimulus to the therapeutic experiments undertaken. Of course, the apparently favorable effect of insulin therapy can only be explained by the fact that the ketones are called forth through lack

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of insulin just as in diabetes. Our knowledge of metabolic pathology up to the present time in ketonemic vomiting is still very inadequate. Yet the little we do know speaks unequivocally against the deficiency of insulin in ketonemic vomiting. In insulin deficiency the carbohydrate utilization in the organism suffers. None of the important symptoms of insulin deficiency are to be observed in ketonemic vomiting of children. The blood sugar is for the most part, if not constantly, considerably lowered. If an analogy can be drawn into consideration, the possibility of a deficiency of insulin in ketonemic vomiting of children is not to be disputed; the whole symptom complex corresponds to the picture which is observed in overproduction of insulin. Clinical experience as well as experiments undertaken by Hillinger and corroborated by several authors, of a favorable influence of administration of carbohydrate on ketonemic vomiting, also speak against an existing deficiency of insulin. From these considerations the conclusion is given for practical purposes that the sole administration of insulin in ketonemic vomiting is not only unfounded but can also be very dangerous. Kelly reports the case of a child who was brought into a condition threatening life by doses of insulin alone. Frei also states that he is against insulin doses without simultaneous administration of carbohydrate. The favorable reports in the literature are not conclusive since insulin was given simultaneously with sugar. In this combined administration insulin is not harmful, but the injections are a burden to the patient in each case and absolutely superfluous.

Abstracts

Remarks Concerning the Measurement of Insulin. Contribution III. — K. Freudenberg and W. Dirscherl. (*Hoppe-Seylers Zeitschr. physiol. Chem.*, **180** : 212, 1929.)

The authors strove in their experiments for an adjustment between an ideal measurement which takes into consideration the natural conditions of the insulin effect and a measurement which may be technically carried out in the course of an investigation. The authors' measurements showed that one of their laboratory units is the same as 1.8 standard units. According to the opinion of Freudenberg and Dirscherl the crystallizing insulin preparation is the principal bearer of the activity of the technical preparation. They consider insulin as an albumin substance with prosthetic grouping, which is protected by the insulin. If the latter is broken up, then more active preparations of slighter durability may very well occur, as Dingemanse describes them.

Hyperthyroidism and High Blood Pressure. — O. Laufer. (*Med. Klin.*, **25** : 218, 1929.)

The reports concerning thyroid action on conditions of blood pressure in hyperthyrosis are not very numerous but very diverging. The author observed several cases which show that the simultaneous occurrence of hyperfunction of the thyroid and rise of arterial pressure not infrequently is noted. An intimate relationship between both phenomena is assumed although its mechanism in all cases may not be determinable and similar. Even though we have hitherto bestowed consideration predominately on the adrenal system and the sex glands in the discussion of blood pressure conditions, it is shown that in such cases that the thyroid and its hormone also acquire considerable significance as hypertonizing factors.

Concerning Treatment of Dysmenorrhea. — W. Liepmann. (*Med. Klin.*, 25 193, 1929.)

The author recommends that each severe case of dysmenorrhea be treated with narcotic therapy through application of a cocain pledget of cotton and that another treatment be tried only when this fails. It is assumed that the diversity of causes also parallels a multiplicity of therapeutic agents and preparations must accordingly be chosen which possess several hormonal components. The author chose a mixture of placenta, corpus luteum, pituitary and ovarin and placed especial value on atropin for uterine spasms. Belladonna is used as atropin preparation, a small amount of

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polamin and a small dose of quinine and salipyrin are added. The finished preparation is administered in the form of capsules. Of 20 cases treated in this manner five became entirely free from pain, 12 showed an essential improvement, one case a transient improvement, two cases remained uninfluenced. Among the patients treated, there were 8 women with inflammatory diseases, displacements and processes of involution.

The Results of Treatment by Liver Diet. — K. Heymann. (*Paris méd.*, **19** : 142, 1929.)

The liver extract prepared by Cohn in America contains the anti-anemic factor in almost pure form. The significance of this preparation consists in that chemistry now requires to take just one more stride to produce the active factor in crystallized form. Cohn's extract seems to be almost identical with Seyderhelm's preparation. This is now being used in secondary anemias and has effected a remarkable improvement of the function of the bone marrow. Of course, one question is still unsolved. It is not yet clear whether a detoxicating substance, a hormone or a vitamin factor is introduced with the liver.

Investigation Concerning the Physiology and Pharmacology of the pH on the Heart. — T. Komiyama. (*Naunyn-Schmiedebergs Arch. exp. Path. u. Pharmakol.*, **139** : 100, 1929.)

In the influence of reaction change of the medium on the ventricle, a reversible change of function and an irreversible destruction of the ventricular tissue may be sharply differentiated. The combined action of acids and alkalis with neurotropic bases (adrenalin) behaves analogous to the cooperation of the reaction with the inorganic ions. A strengthening of the positive inotropic adrenalin action through simultaneous rise of the alkalescence could not be reached.

The Injection Method of Transplantation of Endocrine Glands. — H. Küttner. (*Bruns Beitr. z. klin. Chir.*, **145** : 721, 1929.)

The results of transplantation of endocrine glands are not satisfactory since they are only transient and depend on a brief pharmacologic action which expires at the moment when the dying cells are absorbed. The lifetime of the transplant is, to be sure, different and very

PRESUMPTION

WE have not fallen into the arrogant error of attempting to educate the medical profession. We serve the profession. From the technically educated, scientific body of medical men all of our ideas are derived. The profession has shown the value of a number of active principles derived from the pancreas in the treatment of diabetes. We are merely announcing that we manufacture a product containing these potent principles. It has had a world-wide and successful use. The product is

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limited in all cases: necroses are always found. Küttner is therefore offering for consideration the injection of living tissue pulp. Kurtzahn and Hübener report concerning objection-free results following injections with thyroid tissues in myxedematous children.

Glycosuria. — F. G. Brathwaite. (*N. Y. State J. Med.*, **28** : 636, June 1, 1928.)

The author made a study of a collection of considerable data made by life insurance companies. This study enabled him to definitely determine that certain groups of applicants with glycosuria, on sub-standard plans, have demonstrated a distinctly increased mortality, and that the greater the quantity of urinary sugar, the higher the mortality.

A study of a smaller but more recent collection of data where the selection is based on other factors than qualitative urinalysis, such as accurate quantitative urinalysis after test meals, and blood sugar determinations, shows that (*A*) Groups of cases have been insured whose mortality was in excess of the expected mortality. (*B*) Groups of cases have been insured whose mortality was less than the expected. (*C*) Groups of cases have been declined insurance who were entitled to it.

Therefore, the author believes that for intelligent study with the view of prognosis in cases of glycosuria, not only must the urine be carefully examined after known test meals, both qualitatively for glucose, acetone and diacetic acid, and quantitatively for glucose (to the exclusion of other sugars), and that comprehensive blood sugar determinations be made both fasting and 1, 2 and 3 hours after the administration of 100 gm. of glucose, or the ingestion of test meals known to contain at least a representative load of carbohydrate. Also, in cases of renal diabetes before an entirely favorable prognosis is given, sufficient consideration must be given to the cause of altered metabolic manifestation as evidenced by (*A*) more or less constant glycosuria, (*B*) eccentricities of "threshold," (*C*) excessive dietary regime, (*D*) overweight, if any or all of these features prevail.

Iodine in Goiter. — William E. Johnston. (*Bull. Wayne Co. Med. Soc.*, **20**: 3, Oct. 2, 1928.)

Prophylactically iodine is indicated in endemic districts to prevent simple goiters during adolescence and to protect the fetus during pregnancy. Therapeutically as a curative agent, iodine is indicated for colloid goiter up to about 25 years of age. It is contraindicated in toxic goiter as a curative agent. Therapeutically as a preparatory agent for surgery iodine is definitely indicated in exophthalmic goiter. It may be used with care as a preparatory agent in toxic adenomatous goiter. Therapeutically as a postoperative agent to combat the induced operative hyperthyroidism and to aid during the convalescence in restoring the thyroid balance to normal.

Oöphorogenic and Psychogenic Uterine Bleeding. — M. R. Robinson. (*N. Y. State J. Med.*, **28** : 1036, Sept. 1, 1928.)

In this paper Robinson considers certain gynecic disorders which are the result of ovarian dysfunctions and abnormal psychic reactions. He says that even this incomplete presentation he gives of the subject suffices to show that the pathogenesis of many types of uterine bleeding resides outside the uterine body, and beyond the confines of cellular pathology. The modern gynecologist in order to serve well, must extend the horizon of his activities beyond the removal of benign or malignant tumors of the generative tract or the salvaging of unaffected remnants left by the ravages of Nisserian, tubercular, or post-partum infections; or the repair of injuries of the generative tract sustained during parturition. The modern gynecologist must go further, he must be trained to recognize functional disturbances as readily as he does organic abnormalities, and from time to time invade the field of the psychologist, for the well being of woman depends as much upon a normal trend of her thoughts as upon the physiologic functioning of the rest of her body.

By oöphorogenic uterine bleeding the author means uterine bleeding in which the uterus as such acts as the end organ through which structural and functional disturbances in the ovary find an outward expression. The effects of these ovarian disorders are first transmitted along afferent sensory nerves of the vegetative system to the spinal nerves, then to the paleëncephalon (especially the pituitary), and from there back again along the efferent motor sympathetic fibers (the hypogastrics) back to the uterus, and the endocrines which stand in close relationship to the generative apparatus. The author gives the following types of uterine bleeding as illustrations: 1. Uterine bleeding in the

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new born. 2. Uterine bleeding in extra-uterine pregnancy. 3. Uterine bleeding associated with microcystic degeneration of the ovaries. 4. Uterine bleeding in cases afflicted with carcinoma of the ovaries.

With the introduction of psychopathology into the realm of gynecology the pathogenesis of many hitherto misunderstood and misinterpreted disorders in the sexual life of women, and in their organs of generation, was placed on a scientific basis.

Function of the Ovary. — Frank A. Pemberton. (*New England J. Med.*, **199** : 87, July 12, 1928.)

Pemberton quotes from Frank as follows: "The function of the adult ovary consists in elaborating a hormone which produces two types of cycles. The one we have called the fertile or complete sex cycle, consisting of maturation of the follicle with its attendant tubular reaction (pregravid reaction), ovulation, impregnation, the elaboration of the corpus luteum, nidation and pregnancy. Pregnancy is attended by the formation of a placenta which in turn sends the female sex hormone into the circulation and assures the continued hyperplasia of the uterus and accessory sex organs throughout pregnancy. Its acme is reached with the onset of labor. The other, called the short, infertile or abortive cycle, does not differ from the fertile one until ovulation has taken place, impregnation for one reason or another having been prevented or not occurring. The corpus luteum then involutes rapidly and therefore the acme of the reaction is reached at estrus in the lower forms or at the time in the human female when the female sex hormone is excreted in the menstrual flow. It is, of course, evident and self-understood that the main, in fact sole, function of the female sex organs is for the perpetuation of the species. To emphasize this function of follicles, corpus luteum and placenta, we call them collectively 'the gestational gland.' "

As Pemberton says, there is some reason for believing that the corpus luteum secretes a substance which prevents menstruation because if a corpus luteum is removed at operation, menstruation appears earlier than it should and if it be done during the early months of pregnancy an abortion frequently follows. As he says, one of the most interesting points, in this work is the possibility, by Frank's method of quantitating the amount of secretion in the blood, or differentiating between amenorrhea due to the absence of the hormone and that due to a persisting corpus luteum. Also in distinguishing various types of menorrhagia or metrorrhagia which may be due to over-production of the sex hormone. Further Frank has proved the sex in two individuals where no palpable uterus or ovaries could be found on examination by demonstrating the female sex hormone in the blood.

Pemberton believes that at present the use of ovarian extracts does not give constant results. There is no unanimity of opinion as to whether the extract of the whole ovary, that of the corpus luteum, or that of the ovary without the corpus luteum is the most effective. These extracts are used for a variety of diseases and at times with success. They appear to be of most use at the menopause, both normal and induced by operation or radium, to relieve the hot flushes and other nervous symptoms. He says that in amenorrhea they are unreliable, one reason being that lack of thyroid secretion and the general health play such a large part in causing amenorrhea. In dysmenorrhea they are sometimes useful in relieving the pain, more often in relieving the nervous symptoms, but rarely give complete comfort. They seem to have little effect in menorrhagia. It is generally conceded that hypodermic administration is more effective than oral.

Novak feels that the results of animal experiments do not throw much light on the human because there is so great a difference in the menstrual function. He thinks that the treatment with ovarian extracts is of most value in hypofunction; that both the follicle and luteal extracts should be used but in a proper sequence simulating the menstrual cycle; and that hypodermic administration is much the surer.

Graves summarizes the use of ovarian therapy as follows: It is a near-specific in the treatment of hot flushes and the vaso-motor disturbances of the menopause. It is ineffective in the treatment of amenorrhea with hypoplasia, menorrhagia, and metrorrhagia. It is occasionally useful in essential dysmenorrhea and the molimenal symptoms of dysmenorrhea. It seems to be beneficial in sterility which might be caused by deficient ovulation. The preparations of the whole ovary or ovarian residue are more efficacious than those of the corpus luteum.

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Cretinism, Diabetes, and Pregnancy. — L. J. Witts. (*Lancet*, **216** : 284, Feb. 9, 1929.)

The case is reported of a woman, 22 years of age, who became pregnant though suffering from cretinism and diabetes. Her mother also suffered from myxedema.

The patient was given thyroid and later insulin and responded well to treatment. She became pregnant. Owing to an oversight insulin was discontinued for 6 weeks when she was readmitted to hospital in coma. Under treatment she came out of coma, the blood and urine became normal, and in a few days she was back on her usual diet. The fetal heart was not heard. Labor commenced spontaneously and she was delivered of a 7-8 months fetus which showed early maceration. Her breasts secreted milk.

Diabetes is more menacing to pregnancy than pregnancy is to diabetes. Conception is infrequent on account of amenorrhea, of vulvitis, vaginitis, and cervicitis, and of voluntary prevention. Before insulin at least 50 per cent of pregnancies ended in miscarriages or stillbirths, and the mother ran a grave risk of coma at delivery, puerperal infection, or aggravation of diabetes. Even with insulin the danger is great. The metabolism is very delicately balanced, and supervision must be close to ensure a normal delivery.

Hypothyroidism is a great, but not an absolute, bar to pregnancy. The occurrence of pregnancy in this girl, who suffered also from diabetes which is inimical to pregnancy, is evidence of the completeness of substitution therapy.

Goiter. — John William Shuman. (*Med. J. and Rec.*, **128** : 339, Oct. 3, 1928.)

The examining physician frequently overlooks goiter as a cause for nervousness, heart disease, loss of weight and other disabilities.

Clinicopathologically goiters are: 1, colloid; 2, adenomatous, and 3, exophthalmic. Colloid goiter occurs in the adolescent, especially at about puberty. The gland is usually enlarged symmetrically and has a soft, velvety feel. Iodine, properly given, is a specific. If not properly managed, this type of goiter is quite likely to give rise to further trouble in the form of adenoma. At puberty, during pregnancy and at the menopause a woman is in danger of a developing goiter. This indicates a close relation between thyroids and gonads. Eighty per cent of pregnant women have enlarged thyroids, which is of no pathologic significance. Recent investigations sug that removal of ovaries causes decrease in and toxic secretion of thyroid.

There are two types of adenomatous goi — simple and toxic. The toxic form ca marked symptomatology; the simple is ra a mythical type because it does cause sym toms, although decidedly more mild than toxic form. "Soldier's heart," the tru irritable heart, is secondary to hyperglan lar (thyroid) activity. Many skin lesio yield to the administration of thyroid extra Obese individuals frequently improve wi thyroid feeding but its indiscriminate use these cases is dangerous. The so-called sim adenomatous goiters are like volcanoes whic may erupt on the least provocation. Oft an adenomatous goiter undergoes cys degeneration following the hyperplastic sta Before goiter surgery became so efficie these were more common. Degenerati myocarditis is a serious result of toxic ad omatous goiter.

Exophthalmic goiter produces exophth mos, tachycardia, and tremor, in addition the gland enlargement. Loss of weight, ne vousness, insomnia, anorexia, diarrhea and g tric crises may be present. All depend up the severity and chronicity of the disord Patients have been known to have "burn out" exophthalmic goiters, *i. e.*, the disease ran its course that a cure by nature result This is rare.

With adenomatous goiter the white blo count is usually increased, due to lymph cytosis. The blood pressure is also higher than normal and the left heart enlarged. T metabolic rate is almost always increase but does not reach the high levels so consta ly in exophthalmic goiter. Often the two c ditions seem present in the same individu and microscopic sections often show adeno atous glands with hyperplasia.

Practically the only difference is the pr ence or absence of exophthalmos, and definite adenomatous areas in the gland. T history of the case is of diagnostic significan A goiter which has been present for a num of years and is suddenly productive of to symptoms, is almost certainly a toxic ad oma. Treatment of toxic adenoma is alw surgical; of exophthalmic, medical follow by surgical; administration of Lugol's s tion is of value in the exophthalmic ty Lugol's solution should be used with gr

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are, only in preparation for operation, and then started 2 weeks before; after this it loses effectiveness. It is contraindicated in toxic adenoma because many simple adenomas have been changed to toxic adenomas by the indiscriminate use of iodin.

Benign Hemorrhages of the Uterus. — Henry Schmitz. (*J. Am. Med. Assn.*, **91** : 955, Sept. 29, 1928.)

Uterine hemorrhage is one of the most important clinical signs of diseases of women. The causative, functional and pathologic disturbances are of equal importance, as the indications for treatment and the methods employed should be based on them. This presentation of the subject comprises: (1) the classification, etiology and frequency of uterine hemorrhages based on pathologic physiology and anatomy, and (2) the treatment of benign uterine hemorrhages due to functional disturbances of the uterus and ovaries. The study is based on a survey of 2184 consecutive hospital records and 2126 records of outpatients. The number of benign uterine hemorrhages in this series was about 25 per cent of the total cases admitted. The classification and frequency of the types of bleedings was:

(*a*) Hyperemia: The menstrual flow lasts too long or is too profuse. It is due to uterine dysfunction. The frequency is about 60 per cent of the total benign hemorrhages.

(*b*) Polymenorrhea: The menstrual flow occurs too soon. It is caused by ovarian dysfunction. The frequency is about 20 per cent of the total benign hemorrhages.

(*c*) Metrorrhagia: There is a bleeding independent of the menstrual flow. It is the result of the loss of continuity of the surface epithelium by ulceration, necrosis or rupture of proliferating processes within the genital canal. The frequency of the benign metrorrhagias is about 20 per cent of the total benign hemorrhages.

A diagnostic curettage and microscopic examination of all scrapings are necessary in those cases in which (1) a correct diagnosis by physical examination can not be made, and (2) the hemorrhage occurred in the menopausal period of life. A woman suffering from a uterine hemorrhage should not be treated until the underlying cause has been determined. All uterine bleeding must be viewed with grave suspicion until it has been proved to be benign. In the treatment of benign uterine hemorrhages due to functional disturbances the age of the patient must be considered, the cause removed, and normal function of uterus and ovaries reëstablished, if at all possible.

The contractility of the uterus is stimulated by ergot, hydrastis, extract of the posterior lobe of the pituitary gland and epinephrin. Ovarian dysfunction indicates extract of the anterior lobe of the pituitary, thyroid, the ovarian follicle and the corpus luteum. The removal of the true corpus luteum causes death of the ovum and abortion. Hence the life expectancy of the non-impregnated ovum depends on the corpus luteum. The endocrine extracts should be given hypodermically. Their action is a problematic one, as uniformly good results are not often seen. General management of each case is important.

The menopausal benign bleeding may be treated less conservatively.

Radiation therapy was indicated in 32.31 per cent of the benign functional hemorrhages and 11.03 per cent of uterine myomas.

Relation Between Gall-Bladder Disease and Pancreatitis. — Daniel Fiske Jones. (*New England J. Med.*, **199** : 716, Oct. 11, 1928.)

The frequency of the association of gall-bladder disease and pancreatitis has been estimated at from 20 per cent to 50 per cent, and careful routine examination, as carried out at present, of the pancreas and gall bladder may give a still higher percentage. The great increase in the number of so-called chronic cholecystitis cases is believed by many to be a serious condition that may lead to pancreatitis and many other conditions.

The writer, in this paper, endeavors to set forth clearly some of the clinical and pathological features of what appears to him to be two entirely different types of pancreatitis: 1. Acute hemorrhagic pancreatitis. 2. Cases where the patient has frequently had previous attacks of gall-stone colic, or cholecystitis; he is usually operated upon for gall-bladder disease.

The author believes that gall stones should be removed with the gall bladder when found, if there are no contraindications. He has seen no evidence whatever to prove that the cases of so-called chronic cholecystitis, in which no gross pathology can be demonstrated, and the cholesterol gall bladders have any causative relationship to acute hemorrhagic

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pancreatitis, and if these gall bladders are to be removed, it must be done for some other reason than the prevention and cure of acute pancreatitis. He believes, considering all known facts, that the treatment of chronic pancreatitis should be to remove any source of infection and drain the biliary system. In acute hemorrhagic pancreatitis Archibald's theory should serve as a guide, and drainage of the biliary system established by cholecystotomy, cholecystectomy and drainage of the common duct, or by cutting the sphincter of Oddi. In addition, he believes that the capsule of the pancreas and fatty capsule should be drained.

Emotional Polycythemia. — J. J. Izquierdo and W. B. Cannon. (*Am. J. Physiol.*, **84** : 545, Apr., 1928.)

Emotional excitement (of a cat in the presence of a dog), for 1 minute, is quickly followed by a pronounced increase of the red corpuscles of the blood. In 15 observations of increases below 30 per cent the average increase was 20 per cent. The increases are far beyond the variations occurring in the usual quiet existence of the animal. The maximal increase is immediately after the minute of excitement; after 5 minutes a fall has started; and within a half-hour the former state has been restored. If the conditions which usually cause excitement fail to do so, the polycythemia does not occur.

Hematocrit and hemoglobin determinations do not show such great increases as does the erythrocyte count; this is explained by a larger percentage of small corpuscles in the blood after excitement.

Emotional polycythemia fails to occur after removal of the upper abdominal sympathetic strands and bilateral severance of the splanchnic nerves. It may even be replaced by a lower erythrocyte count. If only the liver among the upper abdominal viscera is left innervated, excitement causes no noteworthy hyperglobulia. After section of the nerves to the spleen excitement for one minute does not produce polycythemia; prolonged excitement with struggle may occasionally increase the erythrocyte count.

The above research was undertaken to determine, if possible, whether the spleen, instead of the liver, might be the source of emotional polycythemia. The authors ask — do the adrenal glands play an essential rôle? If not, do they play any rôle — are they capable of producing any effect on the corpuscular content of the blood? In the experiments the adrenal glands were active. An irregular effect of secreted adrenin and of injected adrenalin are attributed to variable concentration of the blood in the denervated spleen. Inactivation of the adrenal medulla was found to have no marked influence on emotional polycythemia.

From their studies the authors conclude that the liver is not a significant factor in emotional hyperglobulia. Evidently the spleen is the immediate cause of polycythemia.

Dextrose-Insulin Treatment of Shock. — Preston A. Wade. (*J. Am. Med. Assn.*, **90** : 1859, June 9, 1928.)

The author found that dextrose administered intravenously with insulin subcutaneously in cases of shock gave results more satisfactory than could be obtained in cases treated by saline or dextrose solution alone. Cases of traumatic shock treated early responded most readily to this treatment. Cases of post-operative shock treated in this manner showed marked improvement.

The optimal dosage is 1000 cc. of 5 or 10 per cent dextrose with 1 unit of insulin to 3 gm. of dextrose. Beneficial results are usually apparent after 800 cc. of fluid has been injected. Cases of shock in which the blood pressure is decreasing toward the "critical level" (80 to 90) should be treated immediately before the rapid fall which usually follows with symptoms of severe shock.

The Embryohormonic Relations of the Suprarenal Cortex to Mesothelial Tissues. — Robert C. Moehlig. (*Ann. Int. Med.*, **1** : 828, Apr., 1928.)

The object of this paper is to show that the suprarenal cortex secretion has a selective action on mesothelial tissues. The important mesothelial tissues, sex glands and skeletal muscle are influenced by the state of the suprarenal cortex. Both the mesenchyma and the allied mesothelium through the suprarenal cortex are influenced by the pituitary gland.

Undescended Testicle. — Herbert W. Meyer. (*Surg., Gynecol. and Obstet.*, **44** : 5[illegible] Jan., 1927.)

The exact etiology of undescended and ectopic testicle has not yet been definitely settled. The histological changes point to the

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fact that spermatogenic cells are present and functionate in about 10 per cent of all cases. The interstitial cells, which have to do with the development of the secondary sexual characteristics, are always abundantly present. These findings are almost constant, and therefore, the undescended testicles should always be saved.

Secondary complications occur. Malignant degeneration is not as frequent as is generally supposed. Fear of this is no indication for orchiectomy. Chronic inflammation, the presence of a potential or real concomitant hernia, practically always present, torsion of the spermatic cord, and strangulation of the testicle, are occurrences so frequent that surgical interference is always indicated. Pain is the most frequent symptom. In adults psychic disturbances may occur on account of the depression that comes from the knowledge and fear of abnormal sexuality.

The best time for operation is before puberty, between 8 and 10 years of age in patients with unilateral undescended testicle, and earlier in bilateral cases.

Histological Study of the Thyroid of the Guinea Pig in Experimental Scurvy. —Katherine D. Harris and Erma A. Smith. (*Am. J. Physiol.*, **84** : 599, Apr., 1928.)

As a result of scurvy the thyroid gland shows an increased amount of interfollicular cells, a decrease in colloid, an increase in the number of vacuoles, and a lengthening of the cells lining the follicles, the degree of change depending on the length of time the animals survive the scurvy-producing diet. Acute starvation of guinea pigs reveals no changes in the thyroid by the present method. The results are interpreted as an indication of pathology in the thyroid as a consequence of vitamin C deficiency.

Cod Liver Oil in Parathyroid Tetany. — John C. Brougher. (*Am. J. Physiol.*, **84** : 583, Apr., 1928.)

The addition of cod liver oil to a mixed stock diet for thyro-parathyroidectomized dogs delayed the onset of tetany and lessened its severity when it did occur.

Serum calcium in control and in test animals dropped to the tetanic level but tended to approximate the normal in 30 to 40 days in the animals given cod liver oil.

The point is further confirmed that low serum calcium is not always accompanied by tetany. Cod liver oil relieves tetany and benefits parathyroidectomized dogs either by improving calcium absorption, mobilizing body calcium, or increasing the ratio of ionized to unionized calcium. Thyro-parathyroidectomized animals have been carried through estrus, pregnancy and lactation by the addition of cod liver oil to the stock diet.

The Climacterium in Males. — H. Lyons Hunt. (*Med. Times*, **55** : 75, Apr., 1927.)

The ebb of sexual activity and a critical period of life is common to man as well as woman. Facts prove that the secretion of semen diminishes greatly in quantity as well as in its fecundating power, at about the age of 60. Exceptions are on record of men whose procreative power has been prolonged to the age of 90 or 100, but these cases are exceptional.

There are pathological changes which have been termed "climacteric diseases." Paul asserts that prostatic enlargement in advanced life is the result of an involution change comparable with involution hypertrophy of the breast of the female at the climacteric period. Investigation has led to the belief that all activities of the body — muscular, glandular and visceral — are controlled and regulated by the nervous system. It has been assumed that the ductless glands and their internal secretions play an important part in sustaining the equilibrium of metabolism. The gonads have an internal secretion which acts upon the metabolism to stimulate it in each sex in a specific manner.

There has been too much confusion in speaking of the sex life of man. It is invariably referred to in a general way to include under one heading various phases, namely, sex desire, potency and virility. Until each of these conditions is taken up as an individual entity, the confusion will persist. Each one of these conditions may be present or absent without marked relationship to each other. Hunt cites cases which illustrate this. Also, it is known that there are cases where the testicles and the prostate are normal, but the posterior portion of the pituitary gland becomes involved pathologically and an impotence develops. In association with many pathological conditions, impotency may develop; also, loss of sex desire, loss of virility develop, and yet the testes and prostate remain anatomically unaltered. During the

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climacterium acute and chronic diseases are attended with more than the usual dangers because the powers of resistance are less competent then to battle with the infective or toxic invasion.

Certain climacteric diseases stand out on account of their frequency. Arteriosclerosis is to be regarded as physiologic in a man past 60, though there are certain factors which hasten its development, such as syphilis, infectious diseases, rheumatism and gout. Aortic arteriosclerosis is the most frequent of the arterial degenerations occurring during the climacteric. Just what relation arteriosclerosis has to the endocrine glands is not known. In a series of four hundred cases of transplantation which Hunt performed were a number of cases of arteriosclerosis associated with high blood pressure. He cites cases in illustration. Following transplantation the blood pressure dropped to almost or quite normal where it remained until the transplanted tissue began to be absorbed when it started to rise. This has also been the experience of Stanley and Voronoff. The earliest cardiac change is a cardiac hypertrophy. The chronic endocarditis which is frequently seen in the male climacterium is simply part of the arteriosclerosis of this period. Among other so-called preferential diseases is cancer, which, according to Cohnheim's theory, arises from faulty embryonic development, embryonic cells remaining dormant until later life. The frequency of cancer at this time would strongly suggest an endocrine basis for these abnormal cells, or, at least, the malignant cells receive a nourishment from the abnormal chemicals which are floating in the blood stream at this period. It is known that grafting of cancer cells is not successful in young rodents, but cancer grows with avidity if cells are grafted from one ageing rat to another. It is also known that in gonadal transplantation experiments on rodents, organs which appeared shrivelled and aged will take on the appearance of youth and health within several weeks of a transplantation.

All the climacteric diseases, whatever their nature, are the manifest symptoms of the failure of some governing power regulating the organic processes, and are, as far as present knowledge goes, connected with the dysfunction of the glands of internal secretion. All the physiological changes mentioned by Hunt can be artificially produced. When this is done they occur in a much more aggravated form. Many of the organic disturbances occurring during the climacteric virile are to be regarded as physiological processes, which, under certain circumstances become pathologic. Many authorities ascribe a deeper significance and greater seriousness to physical deteriorations incident to the male climacterium than to those observed during the menopause, because the death rate of man is in such an extraordinary excess over that of woman at the menopausal period. More serious than the physical changes, however, are the mental disorders which may manifest themselves during and after the male climacteric. Loss of memory, loss of self-control often leading to hysterical and emotional conditions, neurasthenia, anxiety neurosis, incapability of concentration, hypochondriasis and suicidal impulses may develop during this period. There may be introspection, with natural fears and unnatural phobias. As a rule the libido, and also potency, decreases, though sometimes there may be a considerably increased libido. Climacteric men often complain of disturbances during coitus, such as orgasm without ejaculation, ejaculation without orgasm, ejaculatio precox, or ejaculatio deficiens. The most distressing manifestation of the climacterium virile are deviations from the normal vita sexualis. Frequency of sexual perversions are greater after puberty than before. This frequency increases with advancing years. The frequency with which climacteric men plunge into sexual debauchery and commit erotic follies challenges the profession to search for an underlying physical cause for such conduct. Lydston advances the theory of a perversion in the quality and quantity of the endocrine secretions, and that the point of departure is to be found in the testicular cells of Ledig, with an aberration of the sex hormone. The vicious circle once established, all of the endocrine secretions play their part.

While Hunt, as a result of his experience believes implantation of gonadal tissue to be the most logical treatment for diseases during the climacteric period and due to the changes taking place at that time, he does not believe nor contend that transplanted gonadal tissue is a true transplantation, but is a transplantation of tissue which is going to be absorbed in a short time. It may last a few months to a year or a little longer, depending

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on the condition of the patient, and in some cases will have to be repeated if the good results are to persist. When gonadal tissue is transplanted, the operator transplants gonadal tissue, composed of thousands of endocrine-producing cells, endocrines which are deficient, especially at the climacteric period of life. During the absorption of this tissue, these endocrines are also absorbed, and supply the body with that which is most vital and necessary to prevent the depredations that the patient is undergoing from their deficiency.

Further Contribution on the Question of the Variability of Hormone Action. — Electrodialysis and Insulin. — H. Zondek and H. Ucko. (*Klin. Wochenschr.*, **5** : 1861, 1926.)

Statement of the theory of the method. Insulin loses its normal activity through electrodialysis. It is also possible for it to lose completely its blood-sugar lowering activity, although there can appear qualitative changes in its type of action. Thus the authors in a series of trials observed that a demonstrable, insignificant and transient decrease in blood sugar followed a relatively marked rise of blood sugar. Also in the experiments in which the blood sugar lowering effect was completely preserved, after 2 to 3 hours, following the injection, there appeared a rise in blood sugar.

The question concerning the manner in which the profound change in insulin action takes place, can of course scarcely be answered with certainty. Our first thought will be of physical surroundings within the insulin molecule, somewhat in the sense recently accepted by Kendall for thyroxin under certain circumstances. The authors believe that for the purpose of regulation of its biological reactions, especially of the physiological term of cell functions, not alone the means for alteration of the colloid condition of the cell is at the disposal of the organism, but that here also the modification of the secretion acting on the cell, in structural as well as biological relations, enters the problem. This point of view should also be significant for clinical pathology. Thus, it is known that there are a number of diabetics who remain refractory to insulin. On the basis of the author's investigations, this need not be especially surprising. Slight anomalies of the colloid condition of the cell, the most delicate disturbances of the osmotic and electrical forces playing on the cells of the organ affected, are sufficient to transform the efficacy of the secretion or preserve it, even when it is formed in sufficient amounts in the organism or given up to therapeutic uses.

Hematuria During Treatment with Insulin. — A. V. Neale. (*British Med. J.*, **3531** : 442, Sept. 8, 1928.)

Because of the rarity of hematuria occurring in diabetic patients under insulin treatment Neale reports a case in which it occurred in a boy aged 5 years.

The points of interest peculiar in this case are: (*a*) that the hematuria was extreme but of very short duration; (*b*) the rapid return of the urine to the normal; (*c*) the hematuria occurred 2 days after the last dose of insulin; (*d*) there was at this time only a slight ketosis.

Clinically this case did not appear to be one of nephritis. The benign nature of this urinary abnormality was apparent in this case and is in accord with observations made in other cases by Lawrence.

Concerning the Thyroid Function Following Removal of Goiter. — B. Breitner, E. Nobel and A. Rosenblüth. (*Mitt. Grenzgeb. Med. u. Chir.*, **39** : 45, 1926.)

Follow-up investigations on 32 cases, in which in the last 3 years owing to impediment to breathing only resection of the goiter was carried out, were made by means of Krogh's apparatus. The result may, therefore, be summed up in the statement that following extensive resection of goiter with a good operative technique, signs of decrease in function in the sense of a hypothyroidism are not to be feared.

On the Activity of the Posterior Lobe of Human Pituitary. — W. Lampe. (*Arch. exp. Path. u. Pharmacol.*, **115** : 277, 1926.)

In order to investigate the activity of human pituitary glands, these were removed shortly after death, the posterior lobe cut up in acetone and preserved on ice. On the next morning, the remaining acetone was removed, and the pituitary left in the exsiccator for 24 hours at 37°. On the third day the pituitary preparation, by this time already considerably dehydrated and defatted, was extracted for 3 hours with acetone in a Soxhlet apparatus. For the production of an

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extract the substance was then pulverized after evaporation of the acetone, in the agate mortar, dried for 24 hours in the exsiccator and then 1 cc. of 0.25 per cent acetic acid added per mg. of substance. The average weight of 20 human pituitary posterior lobes amounted to 0.11 gm., the yield 12.3 mg., therefore, about 11.5 per thousand. The blood pressure effect was tested on cats. An elevation of 10 mm. Hg was regarded as stimulation threshold. The still active amount oscillated between 0.01 and 0.2 mg. desiccated substance.

The antidiuretic effect was investigated on dogs with urinary fistulae in accordance with the well known method of Kestranek, Molitor and Pick. The still active dose with antidiuretic effect lay between 0.025 and 3 mg. desiccated substance. The uterus effect was tested on isolated guinea-pig uterus. 1:2 millions to 1:700 millions (referred to dried substance) was shown to be the effective marginal concentration.

The results of investigation yield therefore an extraordinary variation in active substance in the pituitary. The pituitary seems to be very resistant to external influences. The activity of the extract bore no relation to the time which elapsed between death and the removal of the pituitary (from 3½ to 27 hours after death, removal had taken place). The antidiuretic and uterotonic effect always paralleled the individual preparations. It could not be determined what relations there were between activity and the different diseases which the patients succumbed to. It was noteworthy, however, that an active preparation was derived from one woman who had been castrated years before.

The Clinical Value of Interferometric Blood Analysis in Polyglandular Endocrine Disturbances Especially for the Significance of Psychic and Constitutional Anomalies. — F. M. Groedel and G. Hubert. (*Münch. med. Wochenschr.*, **73** : 1738, 1926.)

Through the interferometric blood analysis by Paul Hirsch's method we have succeeded in ascertaining quantitatively to a positive degree the organic break-down of each gland and in deducing from the figures obtained the functional disturbance in particular and the degree of the functional disturbance. This method held good in endogenous obesity and the thyrogenous diseases. This condition induced the authors to employ the method in cases in which they considered the so-called constitutional anomalies as a sequel to internal secretory disturbances, in the expectation of ascertaining the actual functional disturbance from the quantitatively different organic decomposition values. Among other things they also succeeded in actually showing that slight psychic disturbances, to be inserted clinically into no disease group, accompanied similar changes in the internal secretions.

Among others, the authors describe the case of a mother and daughter. The mother showed mild psychopathic characteristics. Palpable clinical deviations were lacking. The patient gave the impression of a constitutionally inferior personality, probably consequent to disturbances of the internal secretions. The interferometric blood curve showed very clearly that this suspicion was correct. It showed a quite extreme functional disturbance of the thymus. Obviously, the organ persisted owing to excessive hypofunction of the ovary, and was hyperplastic. Whereas, otherwise, from the high decomposition value of one gland one would infer a hypofunction resulting from a diseased change of this gland, and the disintegration of cells resulting therefrom, here one must infer increased cellular disintegration through diseased and abnormally increased glandular activity (pituitary) and from the slight decomposition value of the antagonistic gland (ovary), the hypofunction of which is the basis of a hypoplasia. To this corresponds the assertion that the menses are always quite weak and of short duration. Furthermore, in such cases, the increased decomposition for testicle in women is interesting and significant, often a sign of a virile sexual type. *Vice versa*, one also sees in men with feminine inclusions, an elevated decomposition for ovary.

The 12½ year old daughter is very nervous and has not yet menstruated. One has the impression of a psycholability with depressive characteristics. The interferometric curve showed in contrast to the curve of the mother a clearly increased ovarian decomposition value. In the daughter's case, also, however, the testicular decomposition outweighed, as the expression of a virile type. For this reason the cause for the constitutional psychasthenia is to be sought in all probability in disorders of internal secretion.

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If the postulations of the investigators should be corroborated in a great series of investigations, then there would perhaps be found in organotherapy in this field, a rich prospect for the removal of these psychic disturbances.

Pluriglandular Instability Resembling Aborted Form of Exophthalmic Goiter. — Léopold-Lévi. (*Presse méd.*, 35 : 56, Jan. 12, 1927.)

The patient showed signs of aborted exophthalmic goiter, including the ocular symptoms. More exact endocrine examination revealed thyroid instability and suprarenal insufficiency. The whole symptom complex was transformed by suprarenal organotherapy. In this respect, the author studied the importance of basal metabolism, which was decreased in this case; the relationship of this syndrome to tuberculosis and syphilis; the antisyphilitic treatments; the importance of Bouchard's nodules, and of gastroptosis in the exteriorization of congenital suprarenal insufficiency.

Interferometric Investigation of the Endocrine Exhaustion during Pregnancy under Normal and Pathological Conditions (Eclampsia and Hyperemesis Gravidarum). — Hellmuth. (*Deut. med. Wochenschr.*, 52 : 1892, 1926.)

Through the nidation of the fertilized ovum changes exist in the maternal organism quite early, in which, on the basis of recent results of research, the glands with internal secretion take part regularly and legitimately. In order to draw attention briefly to the most important changes in the endocrine glands during pregnancy, the author recalls the already externally visible enlargement of the thyroid in many cases, the typical changes in the pituitary, the broadening of the suprarenal cortex as well as the changes in the ovary which in the beginning of pregnancy lead to cessation of follicular ripening. It appeared therefore to be relevant to undertake investigations to ascertain whether the interferometric method was in a position to give new glimpses in this field.

Diseases of endocrine origin present a very important field for the application of the interferometric method. Since, according to the state of present day research, during pregnancy there is regularly concerned in almost all the endocrine glands a functional increase in the sense of an increased functional glandular activity, an abnormally high endocrine exhaustion is *a priori* to be expected in the interferometric investigation. The investigations of the author have extended to the behavior of the following endocrine organs: thyroid, pituitary, suprarenals, pancreas, ovary, testicle, placenta, as well as incidentally also the thymus and pineal gland. The result of interferometric investigations of this kind was, however, negative, despite the fact that in pregnancy and childbirth in most cases an actual increase of endocrine function is concerned. This result stands in accord with the experiences which the author has collected with interferometry in disease conditions modified by the endocrine glands outside of the gestation period.

Complete Arrhythmia, Cardiac Insufficiency and the Thyroid Gland. Deductions from Medical and Surgical Therapeutics. — C. Lian, L. Lyon-Caen and L. Pollet. (*Presse med.*, 35 : 33, Jan. 8, 1927.)

Various cardiovascular disorders are observed in the course of thyroid affections: cardiac insufficiency and various changes in cardiac rhythm, in particular, complete arrhythmia, which frequently arises in exophthalmic goiter. The authors reviewed all the cases of exophthalmic goiter collected by one of them for the past 15 years (comprising cases of confirmed exophthalmic goiter and toxic adenoma), omitting the cases of aborted exophthalmic goiter. Complete arrhythmia was encountered quite often in these cases, in a proportion of approximately 10 per cent of the cases; but it was not the usual finding. Relative to the frequency with which this symptom was noted in exophthalmic goiter and in toxic adenoma, it appeared to be slightly more frequent in the latter group. The authors also noted that complete arrhythmia in cases of goiter without hyperthyroidism is far from being an exceptional finding.

The pathogenesis of complete arrhythmia in exophthalmic goiter is still under discussion. Today, the tendency seems more and more toward giving to the toxic factor the preponderant rôle. The intoxication seems not only to be the principal cause of Basedowian asystole, but of disorders of cardiac rhythm in Basedowians as well.

These conceptions show that the therapy of complete arrhythmia in exophthalmic goiter should be directed principally against the

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thyroid disease and secondarily against the arrhythmia itself. The underlying treatment of dysthyroidism may be medical or surgical. In accord with the opinion of many others, the authors believe that radiotherapy is the treatment of choice in exophthalmic goiter. They also believe that electrotherapy is good adjuvant treatment especially in intervals of respite from radiotherapy. One of the authors' patients, having had her exophthalmic goiter cured, returned 6 years later with complete tachy-arrhythmia. This disappeared in the course of a treatment by thyroid radiotherapy. This observation showed that in a case of exophthalmic goiter with complete arrhythmia, radiotherapy may be expected to ameliorate not only the cardinal symptoms of the disease but the complete arrhythmia as well.

As other medical agents, the authors recommend iodin, sodium borate and Coulaud's serum. Radiotherapy has the disadvantage of leaving adhesions capable of embarrassing surgery later: it is, therefore, rarely to be employed in toxic adenoma. In any case, the authors would not delay recourse to surgery in cases of toxic adenoma as much as in cases of exophthalmic goiter.

To the medical prescriptions directed against hyperthyroidism, we may add those which are addressed directly to the auricular fibrillation: digitalis, rest in bed, both of which have effected the disappearance of the arrhythmia. The only remedy, however, which can be counted on to relieve the complete arrhythmia is quinidine sulphate.

Surgical treatment was undertaken by the authors in cases of complete arrhythmia due to exophthalmic goiter or toxic adenomatous goiter, only after the failure of prolonged medical treatment in exophthalmic goiter; but it was employed either at the first onset or after a brief medical treatment in toxic adenoma.

With regard to the relationship between complete arrhythmia and myxedema, the authors did not observe a single case in their series. They did, however, observe seven cases of complete arrhythmia in simple goiter. The authors are convinced that simple goiter, without undergoing Basedowian transformation, constitutes in many cases, the source of formidable cardiac attacks in the future, among which may be numbered cardiac insufficiency and complete arrhythmia, symptoms which appear especially to arise from an intoxication of thyroid origin, a thyrotoxicosis.

In cases of complete arrhythmia or cardiac insufficiency complicating goiter which clinical examination does not show to be toxic adenoma, if the usual medical treatment does not give satisfactory results, recourse must be had to enucleation of the goitrous lobe. Even if the medical prescriptions have improved the patient's condition, the authors tend strongly toward advising partial thyroidectomy anyway.

Finally, in all varieties of goiter, whatever the clinical form under which it evolves, physicians and surgeons ought to familiarize themselves with the idea of complete arrhythmia and cardiac insufficiency which are in many cases dependent upon an intoxication of thyroid origin and in which in order to prevent and cure the cardiac attacks, the thyroid lesion must be treated medically, or if necessary, be, surgically.

Interferometric Investigations on the Question of Old Age Especially in Consuming Arteriosclerosis. — F. M. Groedel and G. Hubert. (*Deut. med. Wochenschr.* **52** : 1981, 1926.)

According to Lorand, the final cause of premature old age is the degeneration of the various endocrine glands. Therapeutically he recommends therefore the administration of hormone extracts and iodin, the most important ingredient of the thyroid, as actual specifics against manifestations of old age. The authors themselves have observed patients with sclerosis, in whom frequently after years of good health, a sudden break-down of strength was noted among manifestations which resembled endocrine disturbances thoroughly. The disease pictures differed widely. Sometimes there were symptoms suggesting of hypofunction of the thyroid gland, and at other times, of hyperfunction of this gland. In one case, there existed lessened, in another abnormally increased sexual impulse, etc. On the whole, they had the impression that the sclerotic changes in general do not greatly injure the vitality of the individual or endanger life energy and duration of life. Only when the changes develop with excessive rational speed and intensity in definite organs does there result a general break-down. This fact is very well known among other things from coronary sclerosis, sclerotic contracted kidneys, etc. The above mentioned diseases

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pictures are to be interpreted as no other than sudden aging of the entire body, owing to the deficiency of an important gland.

Since the interferometric modification of the Abderhalden reaction (as Paul Hirsch has suggested it) makes it possible to specify the disturbances of the endocrine system, the authors endeavored to solve the question with this method. They investigated for carcinoma (interferometrically) the blood from a 78 year old woman, who had been entirely healthy until the appearance of exceedingly rapid senile deterioration. The carcinoma suspicion was shown to be unfounded; on the other hand, the thyroid, ovaries and pituitary were found to be abnormally exhausted, and indeed, all three glands to an almost identical degree. From this finding, the authors infer a hypofunction of these three glands — in the aforesaid case as sequel to a senile change.

That the hypofunction of the sexual glands actually corresponds to a strongly elevated interferometric exhaustion value, the following two cases can demonstrate: A man aged 53 years, with excessive hypertonia, physically very strong, with no clinical symptoms of renal disorder. Thrice in the course of the last 2 years, he has had attacks of cerebral pseudo-embolism. Each time the symptoms receded after some hours. The patient remarked that he had never had great sexual desire, and that recently libido had been almost extinguished. Besides a high rate of decomposition for the sclerotic kidney and a still somewhat higher rate for the normal kidney — the authors infer a compensated, non-progressive renal sclerosis — the decomposition rate for the testicles surpassed by far that of all other endocrine glands. There is, therefore, obviously a dysfunction or hypofunction of the testis in this case.

The second case was that of a female patient, aged 45 years, likewise with sexual hypofunction. By interferometric investigation, the decomposition rate for the testicle was shown to be abnormally high. On the other hand, in a greatly reduced sclerotic patient (55 years), marked hystero-depressive neurasthenic characteristics were observed. The nervous symptoms suggested a beginning cerebral sclerosis. Clinically, slight dilatation of the aorta, albumin traces in the urine and hyaline cylinders were found. The interferometric investigation showed a slight decomposition rate for testicle, a strikingly increased decomposition rate for thymus and thyroid and an increase for pituitary. Here, therefore, the endocrine sclerotic disturbance is to be sought entirely outside of the sexual sphere, probably in the thyroid and thymus. The extremely high decomposition rate for arteriosclerotic kidneys is, incidentally, an important hint to revise the clinical diagnosis. In the case described, we may assume pluriglandular sclerotic disturbances, with the exception of the testis.

The authors describe a still greater number of cases, among which some showed considerably increased decomposition rate for the testis, besides increased decomposition rate for other glands, consequently, pluriglandular changes of senile nature. In any case, if we desire to draw conclusions from the interferometric observations in consuming arteriosclerosis, we can call especial attention to two factors as fairly well demonstrated:

(1) In consuming arteriosclerosis very frequently a marked cellular deterioration of the endocrine organs may be determined, and with it the hypofunction of the involved glands.

(2) All glands can be attacked by this senile decomposition, in some cases only one gland or one gland predominately, in other cases several glands at the same time.

A Case of Melancholia Associated with Vitiligo. — C. J. Parhon and M. Désévici. (*Bull. mém. Soc. méd. hôp. Paris*, **43** : 39, Jan. 27, 1927.)

Recently the authors had the opportunity to observe a patient presenting melancholia simultaneously with patches of vitiligo and leucotrichia. The patient was a woman, 35 years of age, who entered the hospital owing to psychic disturbances of depressive character. The authors question whether there is a relationship between the psychic syndrome and the cutaneous dystrophy. Syphilis has often been incriminated in the etiology of vitiligo but no symptoms of syphilis could be observed in the present case; laboratory analysis and the patient's history were also negative in this respect. The authors then turned their attention to disorders of the endocrine functions.

Vitiligo has several times been seen in association with exophthalmic goiter. Thyroid disorder is, in fact, able to give an explanation for the depigmentation of the hair and Sainton and Peynet have looked upon vitiligo as a prolongation of leucotrichia.

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One of the authors (Parhon), in collaboration with Savini, has already directed attention to the depigmentation of feathers under the influence of thyroid treatment, and the vitiligo of Basedowians, as well.

The patient in the authors' case is not an exophthalmic goiter case; but she may be considered as hyperthyroid: the slight tachycardia, the brilliancy of her eyes, the enlargement of the thyroid gland, pulsations of the carotids, crises of diarrhea, suggest this.

Researches of Laignel-Lavastine as well as those of one of the authors have shown the importance of the thyroid factor in melancholia. In conclusion, the authors believe that the presence of vitiligo and melancholia in their case is not a simple coincidence. The two disorders can be explained by a common pathogenetic factor represented by exaggeration of the thyroid function and perhaps also by a certain degree of dysthyroidism.

Suprarenal Insufficiency and Diphtheria. — Lereboullet. (*Presse méd.*, **35**: 137, Jan. 29, 1927.)

The author reports a series of observations which led him to admit the rôle of adrenal insufficiency in severe diphtheria. Experimentation has for some time past brought to light the importance of capsular alterations in experimental toxic diphtheria. Pathologic anatomy shows, in human diphtheria, a high proportion of evident capsular lesions: in one case in five at least, capsular hemorrhages have been found in children who succumbed to malignant diphtheria.

Clinically, the author has joined with Hutinel, Martin and Darré in stressing the significance of observed signs, outside of the secondary malignant syndrome of diphtheria, and raised the hypothesis of adrenal insufficiency at their origin. Since 1922, he (with P.-L. Marie and Leprat, and recently with M. Pierrot) has systematically investigated the hypoglycemia in severe diphtheria. He met with it frequently, and in the 30 cases studied with M. Pierrot, the great majority had a distinctly lowered glycemia, varying from 0.45 to 0.80, which returned to normal with convalescence. This hypoglycemia, which resembles that of Addisonians, seems to form a biologic argument to be joined to the preceding ones in favor of the rôle of adrenal insufficiency in diphtheria.

This idea has an important practical significance. Systematic adrenal organotherapy permits of better treatment and better chance of recovery in severe cases of diphtheri Lereboullet has been able to reduce to le than 20 per cent the mortality from mali nant diphtheria in his service, and he ow this not only to massive serotherapy but t adrenal organotherapy as well. The latte given subcutaneously and by mouth at th same time, gave him very encouraging result They are, however, a valuable measure i malignant diphtheria. If the effects of adrena organotherapy can be regarded as purel symptomatic, owing to its evident cardio vascular action, we must recognize this coe cord of therapeutic action with the other observations and conclude upon the import ance of the rôle of suprarenal alterations in the production of accidents observed in the cours of malignant diphtherias.

M. Lesné, in his service at the Trousseau hospital, observes, as does M. Lereboullet the frequency of suprarenal insufficiency i diphtheria, and like him, he uses adrenalin but in applying it on the nasal and buccal mucosae and in small doses, owing to the sudden shock which it at times occasions. Various symptoms (enlarged liver, tachycardia, etc.) can not, however, be explained by suprarenal insufficiency. Bulbar intoxication is one of the causes of death. Along with suprarenal treatment, he recommends recours to large doses of serum and to adjuvant remedies.

The Causes of Chronic Constipation. — H. Steindl. (*Wien. klin. Wochenschr.*, 39: 1457, 1926.)

In the course of descriptions of the various causes of spastic constipation, the author draws attention also to those forms of con stipation which may be traced back to dis turbances of the endocrine glands or which form a constant accompanying symptom of definite diseases of the endocrine glands. The author, for example, mentions the obstinate constipation in myxedema, the retention of feces in positive disease forms, associated with sex gland disturbances (infantilism etc. The type of constipation which one encounters in a group of relatively under developed girls is well known (genital hypo plasia, chlorosis, etc.), of which disturbance of the glands of internal secretion surely are the underlying cause. We may recall the group of young female individuals (16 to 2 years), constantly to be observed, with the

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boundless complex of symptoms, who consult the physician or are brought to him chiefly because of their poor appearance, and a thorough examination of whom (to which Schur also alludes recently in another connection) could determine: chronic, often painful digestive complaints, loss of appetite, most obstinate constipation, headaches, slight rise in temperature, menstrual disturbances, with entirely normal heart and lung findings. The blood findings suggest anemia or chlorosis. Frequently, outside of the existing signs of degeneration, these girls also show hypoplasia of the genitalia, functional weakness, symptoms of the vegetative system (sympathico-vagotonia, etc.).

The constipation appearing in this symptom complex results in symptoms of stoppage and accumulation of feces, pains in the appendix and in the region of the cecum, cecal splashing, sensitiveness to pressure in this region, which when associated with rise in temperature in these patients can easily lead to an incorrect diagnosis of appendicitis and to an incorrectly undertaken operative intervention. In fact, such patients are subjected to appendectomy to no purpose (at times, owing to the false interpretation of symptoms, they are submitted to gall-bladder or stomach operations). After these operations the persistence of the old complaints reveals the false scent of the diagnosis and of the undertaken therapy.

Functional changes in the vegetative nervous system (weakness, conditions of stimulation, and others), which may be attributable to disease of the endocrine glands, lie presumably at the basis of all of these forms of constipation symptoms mentioned.

Advances in Ovarian Hormone Research through a New Specific Test Object. — Fels. (*Klin. Wochenschr.*, **5** : 1729, 1926.)

Recapitulation of the previous investigations in which in particular Allen and Doisy, as well as Zondek and Aschheim have a share. The investigations of the author were concerned with the demonstration of the ovarian hormone in the blood through calling forth the estrous cycle in the castrated mouse. This problem has up to the present been treated only by Loewe. Loewe's method for cell counting on the streak of the vaginal secretion is challenged. In general, work was carried on with 2 cc. serum, since it was shown that when 2 cc. were inactive, 3 and 4 also remained so; on the other hand, when these amounts were active, often a not quite clear reaction appeared with less. The result of the injection was always negative in the non-pregnant. The same result was given by liquor amnii, ovarian cystic fluid and human milk. Concerning cerebrospinal fluid nothing can as yet be said; the result in the first 3 months of pregnancy was likewise negative. In the third to the sixth months, the results were changeable and tended clearly toward the positive as time went on. From the sixth month of pregnancy, estrus was excited in all experiments with the serum. Likewise, retroplacental and umbilical cord blood was positive.

Six hours after delivery the reaction was still present; later, it was no longer present. A conclusion *a posteriori* on the content of hormonal substance of the blood from the transient prolongation of the estrous cycle was rejected since normally estrus admits of great variations.

From the results, it follows that in human beings in the later months of pregnancy, a marked increase of hormonal substances appears in the blood, in which then also the umbilical cord blood takes part. This fact can perhaps serve as support for the view that the placenta is not only the depot but also the site of formation of the hormone, since the other sites of formation, such as corpus luteum of pregnancy and ovarian cortex are only effective in the earlier months of pregnancy in the experiment; so that for the hormone increase in late pregnancy just the placenta still remains left over. Furthermore, the evidence for an hypothesis is brought with it, as it was advanced in the addition to the works of Halban. Through these works we know that in the later months of pregnancy on the one hand the fetal female generative organs grow exceedingly more rapidly, whereas the male organs experience a retrogressive movement. The hormone of the ovary and placenta has been made responsible for it, — the investigations of the author justify this view.

On the Use of Concentrated Solutions of Insulin. — P. Mahler. (*Deut. med. Wochenschr.*, **52** : 1172, 1926.)

Wiechowski, the head of the Pharmacological Institute of the German University at Prague, had produced insulin in concentrated form as early as the year 1923 from various

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elements and indeed of such a strength that 1 cc. contained 100 or 150 units. The patients learned how to compute everything in the shortest possible time and many of them understood it even surprisingly well, so that they were able to calculate exactly the necessary amount of insulin suitable to the different forms of diet. All, however, asserted unanimously that this form of injection was much more agreeable and caused almost no pain. It could be observed objectively that patients who had a poor tolerance for the different brands of insulin, showed neither redness nor swelling as soon as the concentrated preparation was made use of. The only misgiving, the fear of hypoglycemia, falls away of itself, according to the generally confirmed experiences, provided that the physician abides by the decision to deliver insulin only into the hands of well educated patients who understand the dosage of their preparation.

A Case of Diabetes Mellitus in a Child, Treatment of Which with Insulin Influenced Growth Favorably. — Chabanier, Lebert and Lumière. (*Paris méd.*, **16** : 603, 1926.)

The authors report a case of juvenile diabetes mellitus in which growth which had come to a standstill with the appearance of the disease, again took its normal course under the influence of insulin. The case was that of a 12 year old child, in whom diabetes appeared quite suddenly and brought the hitherto normal growth to a standstill, occasioned a marked sudden fall in weight, with deterioration of the general condition. Insulin rapidly cleared away the glycosuria and acetonuria, which have now remained absent for 2 months. At the same time, the general condition improved, weight increased (in 10 months) about 6 kg., and growth again resumed its course.

Such a result is, however, not always to be ascribed to insulin.

Concerning the Use of Intravenous Pituitary Sodium Chloride Infusion in the Treatment of Poisoning with Oleum Chenopodii. — Vogt. (*Klin. Wochenschr.*, **5** : 1638, 1926.)

Severe symptoms of poisoning appeared in a woman who had exceeded the maximum dose of about 12 drops of Oleum Chenopodii. Lavage of the stomach with ricinus oil and the injection of heart remedies did not improve her condition. A high intestinal enema was also without effect, as well as the injection of pituitary. In this critical condition, the author made an experiment with the intravenous infusion of pituitary sodium chloride which he had used for a long time past with advantage in the control of post-operative intestinal paralysis. As a matter of fact he succeeded through the application of 60 gm. physiological NaCl solution and 6 ampoules of pituitrin in bringing about a thorough evacuation in the shortest possible time. The author recommends this medication not only in intoxications with Oleum Chenopodii, but also quite generally in the therapy of other poisonings in which evacuation of the intestine must be striven for and where no other contraindication is present.

A Human Ovum Approximately Nineteen Days Old. — J. P. Greenhill. (*Surg. Gynecol. and Obstet.*, **44** : 493, Oct., 1927.)

Exactly fifty human ova less than 3 weeks old have been described more or less thoroughly during the last five decades. It has been the custom of nearly all authors who have reported young human ova to give the age of their ova in days. Most authors have stated the age with great assuredness. Such positive assertions should not be made, however, because there is no accurate criteria for determining the age of early ova. Many important factors concerned in human reproduction are as yet not fully understood.

Greenhill describes a young human ovum obtained in an aborted decidual cast and gives the measurements. The outstanding feature of this ovum is the unusual amount of invasion of the decidua by plasmodium. There is very abundant trophoblast, especially plasmoditrophoblast, in the intervillous space. There are numerous definitive villi, some of which have begun to branch. Blood vessel anlagen are found in the mesoderm of the chorionic vesicle, the villi, the body stalk and the yolk sac. The few preserved sections of the embryo show a small amniotic vesicle and an embryonic shield lying upon a large yolk sac. In the decidua capsularis is an operculum deciduae which appears to consist of fetal ectoderm and is attached to the chorion laeve by a strand of plasmodium. The decidual reaction is more pronounced in the stroma cells than in the glands. Some of the large veins in the spongiosa beneath the

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ovum communicate with the intervillous space and contain free masses of plasmodium. The development of this ovum tallies with ova considered to have a maximum age of 19 days.

Hypotensive Effects of Insulin. Letter from Paris Correspondent. — (*J. Am. Med. Assn.*, **92** : 573, Feb. 16, 1929.)

P. Gley and Kisthinios, in a report, showed that insulin lowers the blood pressure and that this hypotension is not due to the substance that diminishes the blood sugar but to a distinct hypotensive substance.

In a second report Kisthinios gave the results of insulin treatment in several cases of hypertension. In all the patients the decrease in pressure was accompanied by improvement in their subjective and functional disturbances.

In a third report by R. Giroux and Kisthinios were the results of an investigation of the effects of insulin on angina pectoris in non-diabetic patients. They reported four cases in which this treatment stopped the attacks for several months and brought about a diminution in the opacity of the aorta as shown by roentgenograms.

Utilization of the Calcium of Spinach. — Laura McLaughlin. (*J. Biol. Chem.*, **74** : 455, Sept., 1927.)

Spinach, fed for 6 days as the only food high in calcium in a diet consisting of some of the most commonly used foods produced distinctly positive calcium balances in six out of seven healthy women and calcium equilibrium in the seventh. Spinach furnished 70 per cent of the calcium, and the intake was greater than the calculated requirement for maintenance. It was thought that the repeated use of an unusually large quantity of spinach would emphasize any tendency toward hindrance to calcium assimilation through presence of fiber or oxalates, but no such tendency was demonstrated. Storage of calcium in adult women is assumed to demonstrate a utilization of the calcium of spinach.

Diabetes Mellitus and Concomitant Leukemia. — Jerome Glaser. (*J. Am. Med. Assn.*, **88** : 1626, May 21, 1927.)

The simultaneous occurrence of diabetes mellitus and leukemia in the same person is so unusual that Glaser reports this case. Of four other cases previously reported in the literature three came to necropsy, and in none of these did microscopic examination of the pancreas reveal evidence of leukemic infiltration. Therefore, the simultaneous occurrence of diabetes mellitus and leukemia in these cases, at least, can not be explained on the basis of leukemic infiltration of the pancreas.

In the author's case here described, the pathologic evidence of myelogenous leukemia in the spleen and retroperitoneal lymph nodes, together with the qualitative changes in the blood picture without any marked increase in the total leukocyte count, classified the condition as myelogenous leukemia of the aleukemic type. Another unusual feature of the case was the pigmentation of the skin. Bronzing similar in appearance to this occurs in the so-called bronze diabetes, in which group the pathologic observations showed this case not to belong. Such bronzing does not occur in diabetes mellitus.

An explanation of the unusual pigmentation which occurred in the author's case may be found in the theories of Féréol and Nieskowski and of Paget and Fowler. They believed that pigmentation associated with lymphadenopathy is due to disturbance of the sympathetic nervous system and through this of the suprarenals, by pressure of enlarged abdominal lymph nodes on the abdominal sympathetic chains and ganglions. Another and later theory is that of Peters, who made the suggestion based on work by Eppinger, that an injured liver may be unable to perform its normal function of removing melanin from the circulation and may permit an excess of it to reach other body tissues, thus giving rise to excessive pigmentation.

Blood-Sugar Estimations in the Treatment of Diabetic Coma. — Philip Bayer and A. Victor Neale. (*Lancet*, **216** : 129, Jan. 19, 1929.)

Diabetes mellitus sometimes presents unusual features in childhood. The authors observed a diabetic child who had a blood-sugar of about 40 mg. per cent over a period of a few weeks without any adverse signs or symptoms. They believe that this may not be very unusual in children. They report a case illustrating this and the difficulty it causes in the treatment.

A girl, aged 13 years, was admitted to hospital in a state of semi-coma. The urine contained 6 per cent sugar. She was treated with

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140 units of insulin (in 20-unit doses), and as the urine still contained 1.8 per cent of sugar a further 10 units of insulin were given.

During the period it was not possible to obtain blood-sugar estimations, but 1 hour after the last dose of insulin the blood-sugar was 13 mg. per cent. Clinically the child had passed from hyper- to hypo-glycemia, but still retained the glycosuria.

It was manifest that the renal threshold had been completely disorganized and, for the time being, the kidneys were allowing sugar to escape despite a subnormal blood-sugar. This rendered it essential that further treatment should be controlled by frequent blood-sugar estimations.

After the state of coma had been overcome a great susceptibility to insulin occurred, the blood-sugar being reduced from 283 mg. per cent to 115 mg. per cent with 10 units of insulin, the urinary sugar falling from 3.8 per cent to 2.0 per cent at the same time. This further illustrated the value of blood-sugar estimations.

Large doses of glucose were required to raise the blood-sugar to normal limits, apparently because of the extreme degree of renal leakage and prolonged effect of insulin.

Four weeks after admission the renal threshold for glucose had improved, but had not become normal. A recent re-examination shows the persistence of the abnormal renal threshold.

Cases of Diabetes Mellitus with a Low Renal Threshold. — R. D. Lawrence. (*Brit. Med. J.*, **3552** : 196, Feb. 2, 1929.)

There seems no reason to think that the combination of diabetes mellitus with a lowered renal threshold is not a mere coincidence.

Hjärne has recently published a hereditary study of renal glycosuria which tends to show the absence of any connection between diabetes mellitus and renal glycosuria.

The most likely explanation of these cases is the fortuitous development of true diabetes in cases of renal glycosuria. It is well known that a lowered threshold is fairly common in normal individuals.

These cases seem, on the whole, to follow the same course as diabetes with a normal renal threshold. These cases respond to treatment, apparently, in the usual way but present some difficulty in their management.

It is difficult to see any etiological connection between the lowered threshold and diabetes in these cases. It is highly improbable that the diabetes produces in some way a lowering of the threshold, for any change that is known to take place in diabetes is in the direction of a rise in the threshold.

Mumps Orchitis with Especial Reference to Sterility. — Francis Patton Tw... nem. (*New England J. Med.*, **199** : 1262, Dec. 20, 1928.)

With occasional exceptions, orchitis in mumps is confined to the period of puberty and adolescence. In the majority of cases the orchitis is unilateral, and for some unknown reason, the right testicle is more frequently involved than the left. Wesselhoeft found, from a study of the literature, that out of 1208 cases of orchitis, 209 cases were bilateral. It may be said that out of all cases of mumps about 1 out of 6 has orchitis and that of these orchitic cases about 1 of 6 has bilateral orchitis. In other words, approximately 3 per cent of all cases of mumps develop a bilateral orchitis and hence are in some danger of subsequent sterility. In these cases of bilateral orchitis, there frequently follows a greater or less degree of testicular atrophy.

Opinions differ as to what may be done to prevent the development of orchitis in beginning cases of mumps. Fougerousse states that it was shown at the U. S. Naval Hospital at New Orleans that the early treatment of mumps with convalescent serum is an efficient preventive of orchitis. Cheinisse believes that convalescent serum in mumps is not specific and that certain experiments indicate that normal serum would be just as effective. The author says that in cases of incipient mumps the use of mumps convalescent serum with a view to lessening the severity of the disease and of avoiding orchitis is well worth a trial.

Sterility due to orchitis is often present without any loss of sexual desire or potency and without any abnormality of secondary sex characters. Investigators who favor the use of diphtheria antitoxin and those who favor the use of convalescent mumps serum as means of preventing the development of orchitis, believe that these means, if employed early in orchitis, will help to prevent subsequent testicular atrophy. The author believes that the work done thus far has been insufficient to establish the truth of the matter conclusively. He says that probably the most promising method known at present to pre...

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ent or lessen testicular atrophy is surgical. de adds that the testes are not the only genital organs that may be affected in mumps. Destruction of the epididymis and vas deferens, and atrophy of the prostate and Cowper's glands may also occur.

Sulphur as a Remedy for Diabetes. — Contribution of the Discoverer, Prof. Bürgi. (*Neue Freie Presse*, **22363** : 3, Dec. 17, 1926.)

The discoverer of the new remedy for diabetes, Prof. Emil Bürgi, who in association with Dr. Gordonow made the discovery that sulphur is capable of lowering the sugar content of the blood, reports the following:

About 2 years ago, Prof. Bürgi began to concern himself with the question of how sulphur acts on the metabolism. Sulphur is a substance which has for a long time been prized as a remedy for everything possible and for this very reason has fallen into discredit. For several years past, interest has grown especially because there have been observed definite results in chronic articular rheumatism, bone tuberculosis and skin diseases from sulphur baths. In order to discover the fundamental action, the author investigated the metabolism of animals. He then, in association with Dr. Gordonow and Prof. Wegerlin, determined that in animals which receive sulphur, glycogen increases in the liver, whereas the content of the blood in sugar becomes less and the basal deposit sinks. This all stands in a causal relationship. Since in diabetes, the reverse is the case, *i. e.*, the liver breaks up glycogen which is nothing other than animal starch, too quickly, and sends too much sugar into the blood, this action of sulphur can certainly be employed in diabetes.

The testimony of Abel and Geiling concerning insulin is in part concordant with these experiments, which since that time have been corroborated by other workers. Insulin is a so-called internal secretion, that is secreted by the pancreas and hinders glycogen decomposition in the liver and principally for this reason represents the best remedy for diabetes at the present time. Since it can, however, occasion dangerous secondary phenomena, the milder treatment with sulphur would perhaps be preferable.

The author represents the action as mild and not energetic, so that in general a longer course of treatment should be given. Insulin is not a remedy which definitely cures diabetes, but merely removes the severe symptoms for a time. Insulin has a stronger action than sulphur, but it is possible to give sulphur to patients for months, even years, which can not be the case with insulin. The chemical experiences concerning the actions of sulphur in diabetes are of course not yet sufficient, although on the whole they speak in favor of the correctness of Bürgi's experiment.

Sudden Death in an Eczematous Child with Hypertrophied Thymus. — Houcke and Martin. (*Presse méd.*, **35**:57, Jan. 12, 1927.)

Report of a case of sudden death in the course of an attack of dyspnea in a child of 20 months, very healthy in appearance, but with weeping eczema of the scalp. Autopsy revealed a thymic hypertrophy without compression of the neighboring organs. The thymus weighed 23 gm. and histological examination confirmed the preceding data.

In this case, it seems that the eczema and sudden death may be related to a dysfunction of the thymus. There would, therefore, be a primary interest in keeping a lookout for thymic hypertrophy in eczematous infants, by means of radiography, in order to treat this lesion with radiotherapy or even with surgery.

Specific Dynamic Effect. Pituitary Anterior Lobe and Obesity. — O. Kestner, R. Liebeschütz and H. Schadow. (*Klin. Wochenschr.*, **5** : 1646, 1926.)

The authors could determine that human beings with increased fat deposit had a too low specific dynamic action. Through the administration of anterior lobe of the pituitary, the specific dynamic action could be raised. With pituitary anterior lobe they were able to reduce the corpulency of healthy and diseased individuals, even if but slowly. The lowering of basal metabolism with pituitary anterior lobe, already observed by Liebesny is opposed to this idea, however. If a reducing effect is therefore actually desired, thyroxin and pituitary anterior lobe should be combined. With the combination of pituitary anterior lobe and 0.1 up to 0.2 glandula thyroidea, the authors never observed any complaints whatever in the course of treatment of many months. Still, they hold it correct not to combine the remedy in one preparation, but to give the extracts separately, so that the physician can adjust the treatment.

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Are Insulin and Hydrocyanic Acid Antidotes? — Szolnoki. (*Deut. med. Wochenschr.*, **52** : 1427, 1926.)

In animal experiments, the action of cyanide was inhibited by insulin; after 24 hours a dose of insulin could restore oxidation in severe cyanide symptoms. In any case, it is a task for further investigation to determine the antagonism between insulin and cyanide of potassium.

Until now, those poisoned severely by cyanide were irretrievably lost. Insulin as oxidation promoter was not applied in human beings in similar cases. With a certain plausibility the intravenous injection of insulin can be tried in cyanide of potassium poisoning as the last resort, just as in coma, in large doses (30 units and more) with simultaneous administration of grape sugar.

Suprarenal Migraine Successfully Treated by Organotherapy. — Jacques-Sébillot. (*Progrès méd.*, **3** : 107, Jan. 15, 1927.)

For the second time, the author presented the case of a patient completely cured for the past year by suprarenal organotherapy of very frequent, violent and refractory attacks of migraine of suprarenal origin (five a month). Organotherapy has been discontinued for the past 3 months and the patient has continued on an ensemble of "kinesitherapeutic methods of endocrine stimulation." The whole treatment has given not only cure of the headaches but an actual restoration of physical and moral health, as well.

Treatment of Diabetes with Insulin and Diet. — H. W. Jansen and P. Müller. (*Münch. med. Wochenschr.*, **73** : 1687, 1926.)

Description of the practical application of insulin. With the dietetic-insulin treatment for the purpose of raising the tolerance, the authors obtained a higher tolerance for carbohydrate and calories in the majority of cases than was usually seen in the purely dietetic treatment. With this improvement in tolerance, there was also associated a rise in the general state of health and — especially in patients in a condition of undernutrition — a gain in weight and improvement in strength. A peculiar, not to be underestimated advantage of dietetic-insulin therapy needs to be mentioned: The ketonuria sometimes present at the outset and appearing especially with the institution of diet with restriction of carbohydrate, which can develop in a particularly threatening manner, disappears at once or after several days with insulin treatment. Besides, it was at times shown that the urine sugar had already disappeared while the urinary acetone still remained present for several days. The origin of this acetone is not clear. In every case this ketonuria has no practical significance and soon disappears again.

The authors had favorable experiences with insulin-dietetic therapy in the treatment of tuberculous infections, complicated by diabetes. Of course, this therapy permits of a richer nutrition than through simple dietetic treatment and makes possible an improvement of the state of nutrition and with it an increase in strength, which is of decisive influence for the course of tuberculosis. For the treatment of diabetics with tuberculous complications, higher doses of insulin are frequently required, in order to obviate an exacerbation of the extremely dangerous state of metabolism through the infection.

Treatment of Nephrosis with Thyroidin Tablets (Richter). — L. Jehle. (*Wien. med. Wochenschr.*, **76** : 167, 1926.)

The author refers to Eppinger's communications on the efficacy of thyroid preparations in edema of patients suffering from nephrosis and reports that the cure effected by thyroid treatment, so far as his observations are concerned, may persist for 1½ years without recurrence. Thyroidin increases diuresis, eliminates dropsy and brings about the extraordinarily rapid retrogression of albuminuria in cases with a high amount of albumin contained in the urine.

In one case the author had the impression that the child was draining his hydrothorax. Also, the high recumbent position of the legs was accompanied by striking result in one case (60 per cent albumin).

The author is of the opinion that nephritis and nephrosis are systemic diseases occasioned by the establishment of a circulus vitiosus. Thyroidin treatment breaks this cycle owing to its favorable influence on the tissue.

In another series of observations, the author obtained good results and important increases in weight through the long continued administration of thyroidin (3 to 4 tablets per day) and elevation of the legs, in orthostatic albuminuria.

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On the Objectivation of Sex Gland function. — Anton Lieben. (*Wien. klin. Wochenschr.*, **39** : 1159, 1926.)

Functional disturbances of the sex glands in the male are conditioned either by a primary disease of the organ or secondarily through disturbance of the hormone equilibrium. With regard to the latter type of sex gland insufficiency, we know that disease of almost every endocrine gland is capable of causing damage to the sex glands; that impotence appears in exophthalmic goiter as well as in myxedema, and in pancreatic diabetes. The influence of the pituitary on the sex glands is also evident.

The treatment of impotence offers the physician especial difficulties when the influences of the endocrine glands are not perceptible forthwith. Indeed, Liebesny was the first to demonstrate that it was possible by investigation of energy metabolism to analyse the existing hormone conditions in sex gland disturbances, and according to the declaration of this author, the basal metabolism (consumption of oxygen in resting, fasting condition) as well as the specific dynamic effect of nutrition (increase in consumption of oxygen following supply of food within a definite experimental time) must be investigated in similar disturbances. A decrease in basal metabolism was found in cases with primary sex gland insufficiency. Since this lowering of basal metabolism is, however, also found in primary hypofunction of the thyroid gland, it is necessary to be able to determine by still another method whether the sex gland hypofunction is primary. Liebesny has indeed shown that in cases of primary sex gland hypofunction, low basal metabolism, but often relatively high value for the specific dynamic effect, exists. This rise in specific dynamic action is probably to be related to the pituitary, which arises from the fact that numerous authors were able to determine in animals and in man an essential increase in the size of the pituitary. At all events, the method of Liebesny, in the critical examination of a hormonal genesis, is able to give valuable enlightenment on sex gland disturbance. Hence, before introducing a treatment for impotence, investigations of the energy metabolism must be carried out, since in this way we are enabled (of course, with close consideration of the symptomatology) to obtain important objective hints for the hormonal genesis of a sex gland functional disturbance.

Menorrhagia with an Apparently Normal Pelvis. — J. L. T. Isbister. (*Med. J. Australia*, **2** : 165, Aug. 11, 1928.)

Excessive uterine bleeding often has a constitutional and not a local origin. The real cause is easily overlooked in many cases. Pernicious anemia in the early stages may cause menorrhagia though as a rule the disease is associated with amenorrhea. Osler mentions a form arising after pregnancy and also the occurrence of hemorrhage with this and also in aplastic anemia which so often arises in young women. In myxedema a good deal of confusion has arisen, but it is certain that menorrhagia does occur. The impression that amenorrhea is common has arisen because 44 per cent of the patients are past the climacteric, when the myxedema develops. The possibility of thyroid deficiency should always be thought of in diagnosis. Bell says that exophthalmic goiter, in the very early stages, may give rise to menorrhagia and in the later stages to amenorrhea. There is a menorrhagia with an enlarged thyroid which occurs in girls at puberty and can be controlled by calcium lactate. Sehrt reports that of 85 patients with functional menorrhagia without any pelvic lesions 69 per cent suffered from hypothyroidism. Mitral stenosis is sometimes associated with menorrhagia. Masturbation and sexual excess may cause menorrhagia. Another cause is superlactation. The treatment here is to wean the child and give good doses of calcium lactate. The author adds that during the malignant influenza epidemic of 1919 a very large percentage of women suffered from menorrhagia.

Shaw has shown that with inflammatory conditions in and around the ovaries the cyclical functions of the ovary are not inhibited, but on the contrary menorrhagia is common. Histologically there is increase of lutein tissue in the corpora lutea and this leads to increased menstruation. No less than 38 per cent of patients with pelvic infection suffer from menorrhagia. The peritonitis may come from the appendix as well as the tubes; if from the upper or peritoneal aspect it is less likely to cause menorrhagia, than if it came from below, because when from below, the uterus itself will be infected and be more likely to bleed. And so the ovaries, fixed and matted with adhesions,

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often cause menorrhagia. Very slight pathological changes in the ovary may produce most severe menstrual changes. The corpus luteum plays the part of an organ of internal secretion and influences the thyroid and pituitary. Many of the cases of functional hemorrhage so-called, no doubt, fall under the heading of menorrhagia due to unrecognized constitutional causes and some also are due to ovarian pathological causes. Idiopathic or essential or functional menorrhagia, is commonest at puberty or the menopause. While there is no obvious pathological cause, yet there must of necessity be some pathological state causing it.

Whitehouse has demonstrated that with the functional or essential menorrhagia of puberty and the menopause there is hyperplasia and consequent overaction of the ovary, causing a too frequent period. Consequently curettage often does no good because it can not alter the ovarian condition. Some good may be done by inhibiting not the ovary, but the accessory sex glands, the thyroid or the pituitary. X-rays applied to the thyroid may be beneficial and Whitehouse has been using injections of extracts of corpus luteum. One should not be in too great a hurry to cure such patients. It takes time for the various sex glands at puberty to settle down and accommodate themselves to each other and work steadily and in harmony. In a second class patients suffer from periods that are not too frequent but too long and also without clots like the former class. These are now thought to be due to over-activity of the ovary producing too much hormone and making the uterus bleed. Whitehouse says such patients are benefited by curettage and frequently cured. The reason is not quite understood. Novak urges the importance of diagnostic curettage. In many cases it affords a permanent cure and he advised recurettage as the best treatment for young women. There is another class of patients, usually older, who suffer from severe hemorrhage due to an intrinsic uterine cause. Diagnostic curettage in these cases is most important.

Of late years x-rays and radium have been used successfully in many cases of intractable menorrhagia. Many authorities think it is attended with some risk in the young and child-bearing age. Organotherapy, with the exception of thyroid and pituitary have not proved satisfactory according to the author. Corpus luteum, orally, Novak says, is unsatisfactory. Whitehouse uses an injection of corpora lutea.

Menstruation and Working Capacity. — Letter from London Correspondent. (*Am. Med. Assn.*, **90** : 1882, June 9, 1928.)

The Industrial Fatigue Research Board has concluded, after an important research into the effects of menstruation on working capacity, that menstruation as a rule has no noticeable effect on the working capacity of healthy women.

Raynaud's Disease Successfully Treated with Insulin. — L. Blum and A. Weil. (*Presse méd.*, **35** : 89, Jan. 19, 1927.)

A patient, 39 years old, with Raynaud's disease, to whom rest, heat and sedatives brought no relief, was given insulin treatment. At the end of 10 days, there was distinct improvement, which soon changed to a true clinical recovery.

Practical Therapeutics

(*Continued from page 81*)

Finally thyroid therapy performs good service in goiter treatment. It works like iodin in these cases, yet has the advantage over iodin in that it causes the disappearance simultaneously of hypothyroid phenomena frequently appearing in goiter. The presence of exophthalmic goiter symptoms alone represents a contraindication. Outside of the latter, the following contraindications to thyroid therapy are also to be mentioned. Marked lability of the vegetative nervous system, non-compensating defect of cardiac valves, angina pectoris, tuberculosis, chronic nephritis and severe diabetes.

Of great importance is the dosage. In myxedema relatively high doses can be given, 0.2 to 0.3 gm. desiccated thyroid gland daily. In the milder grades of hypothyroidism one half as strong a dose daily (0.1 to 0.15 gm. desiccated thyroid), or the first dose given every 2 days is sufficient. In cases, where the outbreak of hyperthyroid symptoms is to be feared it is advisable to administer merely 0.1 to 0.15 gm. desiccated thyroid extract every 2 days. The thyroid medication must as a rule be used for a long period of time.

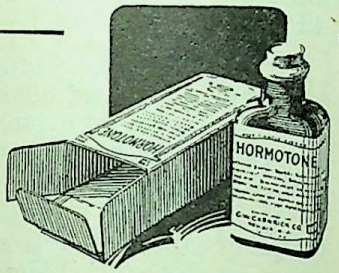
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Pituitary Infantilism with Adiposo-genital Syndrome Due to Tumor of Rathke's Pouch. — G. Guillain and J. Decourt. (*Presse méd.*, **37:** 870, July 3, 1929.)

The authors present a patient of 17 years in whom a syndrome of intracranial hypertension developed at the age of 12 years with progressive lowering of vision ending in complete blindness. When the patient was brought to *La Salpêtrière*, a complete optic atrophy was noted, a midriasis with pupillary inertia and an amaurotic nystagmus. This young man presented a typical adiposogenital syndrome with infantilism and feminism; his height is 1 m. 37; the adiposity is diffuse but especially marked at the root of the extremities, in the mammary regions and on the abdomen and pubic regions; the secondary sexual characteristics are absent; the genital organs are not developed. The psychic state is that of a child of 12 years. Basal metabolism is decreased to 0.49 per cent. There is no polyuria; cerebrospinal fluid is under great tension. Radiography shows a noticeable increase in width and depth of the sella turcica with resorption of the posterior clinoid apophyses; moreover, small intra- and sub-sellar spots characteristic of tumors of Rathke's pouch are observed.

Tumors of the craneopharyngeal pouch are amenable in a number of cases to a surgical intervention by transfrontal route, for radiotherapy which is successful in pituitary adenomas is without action on these tumors. This patient would have been advised to undergo an operation if he had not come to *La Salpêtrière* completely blind. This definite loss of vision appeared a sufficient reason for not considering a serious operation the results of which could not be useful.



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The Female Sex Hormone. A Survey. — E. Poulsson. (*Norsk. Mag. Laegevidenskapen*, **90** : 175, 1929.)

The estrous reaction is not quite reliable. Animals are observed — although a positive cause can not be given — which either remain refractory, or some which first show the typical reaction with higher than the usual doses. The reaction is not limited to the vaginal changes; rather it is the uterus which is stimulated to marked growth; its weight attains an amount many times the original and likewise the mammae show not merely enlargement but secretion of milk also. Simultaneous with the genital changes an intense influence on the respiratory metabolism is observable. The "antimasculine" action is very remarkable. In young cocks following 6 weeks of treatment with the female sex hormone there is visible a distinct retrogression of the testis, of the membrum and of the seminal vesicles in comparison with the organs of untreated animals of the same age. The hormone is not species specific. With regard to the chemical properties of the hormone no certainty could be arrived at as yet. For the time being no positive statements are to be made concerning the therapeutic use of the female sex hormone either. Among the cases which seem suitable for treatment with the genital or pituitary hormone may be mentioned: conditions of hypofunction, delayed puberty, infantilism, virilism, premature climacteric. Dementia praecox, in which as a rule there exists an ovarian insufficiency, is also mentioned among the indications. Certain forms of amenorrhea are to be regarded as contraindications, which, as in tuberculosis, diabetes and nutritional diseases, are to be considered as an aid to nature. The valuable raw material for the preparation of the sexual hormone is the urine of pregnant women which also has the great technical advantage that it is free from albumin. Loewe's demonstration of the presence of estrus-inducing substance in the vegetable kingdom is very interesting.

Diabetic Polyneuritis; Remarks on the Action of Testicular Extract. — L. Cornil and Kissel. (*Presse med.*, **37** : 918, July 13, 1929.)

The authors present a patient affected with diabetic polyneuritis in whom improvement of the diabetes was begun by injections of spermatogenetic extract in the face of failure of insulin therapy. Moreover, in the course of the treatment the abolished tendinous reflexes reappeared and the pain was considerably attenuated. They again draw attention to the favorable action of spermatogenetic extract in certain cases of diabetes and recall the earlier works which one of them published on this question with Jochum.

Preparation of a Substance Lowering the Calcium Content and of a Substance Lowering the Phosphate Content of the Serum. — A. Nitschke. (*Zeitschr. ges. exp. Med.*, **65** : 651, 1929.)

The author succeeded in isolating two substances from spleen and lymph nodes of cattle which are not found in the liver, kidneys or muscle and possess a characteristic action. The one of these substances prepared from cattle spleen lowers the serum calcium in the typical clinical picture; the other lowers the content of the serum in inorganic phosphorus.

Spasms of the Esophagus and of the Cardia.—J. Pal. (*Wien. klin. Wochenschr.*, **42** : 765, 1929.)

A possibility of influencing spasm of the esophagus with adrenalin is given. In the beginning adrenalin has a dilating action on the cardia spasm through stimulation of the sympathetic even when subcutaneously used. It is important therapeutically that a few drops of adrenalin introduced into the esophagus immediately before meals, temporarily induce permeability. This is not only possible in stenosis but even in carcinoma. The author was repeatedly able to maintain the stenosis (in stenosis of the esophagus conditioned by carcinoma) permeable to such an extent with adrenalin that feeding was possible or a sound could be introduced. This would be of especial advantage for the treatment if it were possible to lessen the tone locally through medicaments. Such a medicament is not yet known.

Testicular Insufficiency Due to Double Congenital Microorchidism; Grafting by Voronoff's Method; Result. — Delance and Muller. (*Presse méd.*, **37** : 838, June 1929.)

The subject, a man aged 42 years, affected with double congenital microorchidism, presented physical, psychic and sexual signs of testicular insufficiency. In May, 1928, the

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patient underwent a transplantation operation of a cynocephalus monkey according to Voronoff's method. The result 1 year later is remarkable from three viewpoints: (1) Physical (disappearance of asthenia and muscular fatigue, greater aptitude for prolonged work, beginning appearance of secondary sexual characters, hair of mustache and beard, pubic hair). (2) Psychic (sense of well being, changes in disposition in masculine sense) and (3) sexual (greater frequence of erections followed by ejaculations).

Ways of Activating the Formation of Callus in Fractures of the Bones. — K. Glaessner and J. Hass. (*Presse méd.*, **37** : 176, Feb. 6, 1929.)

The authors studied the influence of the thymus and thymus extracts on the consolidation of fractures in young cats. They found that extirpation of the thymus causes a retardation in formation of callus and that extract of thymus accelerates the evolution of fractures. In a second series of experiences they compared the activity of different glandular extracts: injection of albumin, testicular extract, parathyroidin and extract of thymus. Thymus extract had the greatest action on the ossification of the callus. Even parathyroid extract (Collip's) had an action very much inferior to that of thymus extract.

In man thymus extract likewise induced an acceleration in the consolidation of fractures. The medicament can be absorbed in large doses without danger. The authors chose two subjects of almost the same age, in whom they practised a linear osteotomy of the two femurs for defects of osseous formation. In one of the cases they injected thymus, there was no difference at the end of 4 weeks. At the end of 3 months the differentiation was great. The patient who had not received thymus still presented mobility, and radiography with difficulty revealed the existence of a callus. On the other hand the patient who had received thymus extract had a completely consolidated fracture and the callus was solidly formed of medullary substance as well as of osseous compact. This experience leads to the conclusion that thymus extract also activates the formation of callus in man. Since then the authors have studied the action of thymus extracts in a series of cases of retardation of consolidation. All these experiments permit the conclusion that thymus extract combined with a phosphorated substance gives a rapid consolidation of fractures not only in animals but also in man.

Concerning the Heart Hormone of Haberlandt. Report Concerning the Sessions of the Moscow Division of the Russian Pathological Society. — Pawlenko. (*Centrbl. allg. Path. u. path. Anat.*, **45** : 272, 1929.)

The analysis of the substance designated as heart hormone convinced the author (in contrast to Haberlandt) that the extract of the auricle and ventricle exerts an identical action on the isolated heart. The skeletal musculature and a simple Ringer-Locke solution which contains albumin in traces, are identical in action. It was, moreover, established that albumoses, peptones and amino-acids in definite concentration and mixture influence the heart in quite the same way as does the substance designated heart hormone by Haberlandt. Accordingly, it must be assumed that a specific heart hormone does not exist. The action of the aqueous extract of the heart musculature is determined by the albumin products of disintegration contained in it and extractive substances.

Generalized Atrophic Scleroderma with Ovarian-Mammary Syndrome (Genito-Sclerodermic Syndrome) of Tuberculous Origin. — F. Trémolières, J. Lhermitte, A. Tardieu and A. Carteaud. (*Presse méd.*, **37** : 883, July 6, 1929.)

The patient, a young girl of 19 years, was affected with a generalized atrophic scleroderma the evolution of which was regularly progressive and terminated in cachexia and death within about 3½ years. The onset of the scleroderma coincided with the total suppression of the menstrual function and with atrophy of the breasts.

From the histological viewpoint the skin underwent the alterations described under the term of atrophic scleroderma. The sclerosis was complete in the ovaries and breasts and the glandular elements had disappeared. The cortical substance of the kidneys was likewise affected by a marked sclerosis.

This example of the association of scleroderma with ovarian-mammary syndrome enters into the picture of the pluriglandular syndromes which characterize the period of pubertal evolution.

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The authors admit that in this case the scleroderma and the sclerosis of the ovarian and mammary glands, the renal sclerosis, are the expression in the different organs of an identical morbid process set in action by the same etiologic factor: tuberculosis. At autopsy the authors discovered a large bacillary adenopathy next to the pancreas, verified histologically, which remained latent and which was but indirectly manifested by cutaneous and glandular alterations.

Concerning the Place of the Ovarian Hormone in the Hormone Series. — K. Csepai, A. Fornet and St. Pelláthy. (*Endokrinologie*, **3** : 361, 1929.)

The authors have undertaken the investigation of the effect of the ovarian hormone on human beings and tested the action of this hormone on blood pressure, on true adrenalin sensitiveness, on the sugar and calcium content and on the reaction of the blood under diverse circumstances. The following was the result. The ovarian hormone lowered the blood pressure in the majority of the cases even if not significantly. This effect was most significant in some cases of high blood pressure in which within ½ to 1 hour the blood pressure fell from 20 to 25 per cent.

The adrenalin sensitiveness was lowered in almost all cases under the action of the ovarian hormone; still the hormone does not apparently exert so uniform an action in women as in men. The ovarian hormone acts depressing on the tonus of the sympathetic; cases of menstruation and pregnancy form an exception.

In four of nine cases a marked fall of blood sugar picture was perceptible with the ovarian hormone. The action is still more intensive with intravenous administration; but is not significant (max. 0.05 per cent). Moreover, the ovarian hormone lowers the blood pressure. Investigations of the blood pH gave negative result in seven cases.

A Suitable Combination for the Control of the Asthmatic Attack and of Other Allergic Diseases. — M. J. Gutmann. (*Die med. Welt*, **3** : 751, 1929.)

Through the combined parenteral use of ephedrin with suprarenal hormone a remarkable expansion of the treatment of asthma has been accomplished. Whereas the internal administration of ephedrin has been found to be of practical value and very comfortable for the patient and has favorably influenced the asthmatic condition and the interval between the attacks can be widened, the advantage of ephedrin can also be utilized now in the severe acute attack of asthma in that it can be used in injections in combination with adrenalin. The amount of adrenalin in this combination preparation must be chosen so large that it renders possible a complete control of the attack: that is in the majority of cases 0.2 to 0.3 cc. of the solution 1:1000. The action must continue until the action of ephedrin appears. Ephedrin thus prolongs the action of adrenalin, averts the danger of fall of blood pressure below the terminal point and gradually wears away.

Concerning the Hormone of Heart Movement. Pharmacological Investigations with the Heart Hormone Preparation. — L. Haberlandt. (*Pflügers Arch. ges. Physiol. Mensch. u. Tiere*, **222** : 259, 192

Through preliminary treatment with heart hormone preparation the action of digitalis glucosides (strophanthin, digipuratum and squill) on the isolated frog heart beating on the Straub cannula is distinctly heightened. This sensitizing action has already been demonstrated clinically. The resistance of the isolated frog heart placed on the Straub cannula to chloroform and ether anesthesia may be essentially increased through the same preliminary treatment with the heart hormone preparation.

Concerning Organotherapeutic Preparations in the Pharmacopoeias and Their Methods of Investigation. — K. Neumayer. (*Arch. Pharm. u. Ber. deut. pharmacol. Ges.*, **267** : 27, 1929.)

The pharmacognostic methods of investigation of organ preparations outside of thyroid and suprarenal the active principles of which have already been conceived in part, must with great difficulties. Specific chemical reactions are lacking and the identity and purity of the individual preparations are principally to be determined through biologic reactions. The determination of physico-chemical constants, such as dry residue, ash content and extract content must also be desired for the remedies. For some time past works of this kind have been carried on in the pharmacognostic institute of the University of Vienna and microscopic investigations are being made for the determination of the structure

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animal drug preparations from desiccated animal organs and the possibility of a differentiation in this way was tested. Next the source of the desiccated preparations was investigated. A method was also found to prepare microscopic sections of organs in powder form. The microscopic investigation of the sections obtained in this way gave the possibility of differentiation of various cell types. As example of the microchemical characterization the author reports concerning a qualitative demonstration of iodin from thyroid substance.

Ovarian Hormone and Basal Metabolism. — G. Koehler. (*Klin. Wochenschr.*, 8 : 502, 1929.)

As criterium for the activity of the ovarian hormone the determination of the gas exchange has become of great significance. In their castration experiments Loewy and Richter found a fall of 0_2 consumption of about 15 per cent following deficiency of sex gland function, which they could again adjust by administration of specific ovarian substance. Since these observations were reported, the determinations of basal metabolism have also been undertaken during the menstrual cycle, in conditions of ovarian insufficiency or following administration of ovarian substance, and there are numerous experimental and clinical investigations on the subject.

The results of these investigations by Heyn, Klaften and Hornung show that the cyclic processes of ovulation and of menstruation exert no direct influence on the basal metabolism. The above mentioned authors could also determine a slight fall of basal metabolism in mild forms of ovarian insufficiency as well as at the time of the climacteric and following surgical or x-ray castration only in isolated cases, whereas the greater number were associated with normal or slightly raised gas exchange. Lüthje came to the same results.

As regards the investigations concerning the ability of the basal metabolism to be influenced by administration of ovarian substance, a not inconsiderable rise of basal metabolism (of 6 to 23 per cent) was obtained by Brugsch and Rothmann, Heyn, Hannes). Recently at the suggestion of Prof. H. Zondek, in a great number of patients with visible signs of disturbed sex gland function, the authors attempted to influence the gas exchange with ovarian preparations. For these experiments they used the ovarian hormone prepared by B. Zondek and Aschheim in water-soluble form, the activity of which had been demonstrated on the basis of test methods used.

From tables given in the original article it is to be seen that the authors could not discover any influence of administration of ovarian hormone on gas exchange in any of the cases investigated. The fact that in countless cases of objectively visible disorders of the sex glands function, as for example in obese castrates, the author was not successful in raising the gas exchange by ovarian hormone administration or in obtaining an increase in weight, should be a proof for the fact that the sex glands have only a slight importance or none whatever for the occurrence of obesity, and that for this purpose pituitary and thyroid must be ascribed the dominant rôle as regulators of the economy of the organism. It is to be assumed that the adiposity appearing after castration is not directly caused by loss of the sex glands, but arises by way of secondarily induced changes in the pituitary or thyroid.

A Case of Pituitary Dwarfism. — G. Roussy, J. Bollack and N. Kyriaco. (*Rev. neurol.*, **1** : 102, No. 1, Jan., 1929.)

The rarity of cases of pituitary dwarfism induced the authors to report the case of a patient in whom the syndrome was especially distinguished and perhaps connected with a lesion of the pituitary. The patient was a little girl of 12 years, born at term of healthy parents. She has a brother, 18 years of age, normally developed. The onset of the present syndrome dates back to August, 1926, when the child's mother noted a decrease in vision of the right eye with slight strabismus on that side. In March, 1928, the child remarked that the right visual field was diminished more and more. A diagnosis of chiasmic compression was made and immediately directed attention to the arrest of development of the child, manifested for the past 3 years. The authors were struck by the slight size of the girl, who was no taller than a child of nine years. The facies was slightly swollen, the skin of the face and of the whole body was a little dry with tendency to ichthyosis; slight hyperkeratosis of the hairy system was present in the region of the extremities. The hair was also dry. The secondary sexual

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characters were lacking although the child was still very young (12 years). Otherwise there was no disturbance. Her intelligence was especially well developed for her age. She was very affectionate and agreeable. Radiography of the skull showed a considerable enlargement of the sella turcica. Radiography of the various articulations of the extremities showed that there was no retardation of the ossification. General examination revealed nothing in particular. All the reflexes were normal. The child presented no sign of intracranial hypertension: no diffuse or localized headache; no vomiting or nausea; no somnolence. All tests for the study of pituitary syndromes were negative. There was no sugar nor albumin in the urine.

Summarizing, the clinical picture of pituitary dwarfism was complete. The radiographic findings (sella turcica increased in all its dimensions with integrity of the clinoids), the visual disorders (almost complete blindness owing to optic atrophy on the one side; temporal constriction of the other side), gave confirmation to this diagnosis. From the viewpoint of pathological physiology it is therefore a question of a syndrome through affection of the anterior lobe of the pituitary, a syndrome whose pathogenesis is still rather obscure and which should be placed along side of other great osseous syndromes of the anterior lobe. gigantism and acromegaly. The case resembles to a certain extent those reported under the name of pituitary infantilism. It also resembles cases of pure dwarfism without infantilism. Owing to the age of the little patient it is impossible to decide the state of development of the genital organs and of the secondary sexual characters. It is, therefore, difficult for us to say whether or not it is a question of dwarfism associated with infantilism. It is also difficult to determine the nature of the tumoral lesion which has brought about the enlargement of the sella turcica and the affection of the chiasma respecting wholly the nuclei of the tuber. It may be an adenoepithelioma arising in the sella turcica and involving the chiasma directly or by intermediary of the anterior communicant or it may be one of those cystic or solid tumors developed at the expense of Rathke's pouch. This latter hypothesis appears most probable. A course of treatment with deep radiotherapy was begun but is so recent that the authors are unable to judge of its effect. According to the result obtained the authors will decide whether surgical treatment is to be thought of.

Basal Metabolism. — H. Janet. (*Monde méd.*, **39** : 640, 1929.)

Not infrequently small goiters without any symptom of a hyper- or hypo-thyroidism are observed in children. The determination of the basal metabolism may be important therapeutically in such cases. In such a case in a small girl who was apathetic, and remained backward in school, etc., the author obtained a very essential improvement in spirits and in the symptoms mentioned with long continued thyroid therapy.

Hyperthyroidism and Insulin Sensitiveness. — E. Adler. (*Wien. Arch. in. Med.*, **16** : 343, 1929.)

Repeated blood sugar determinations following subcutaneous injection of 5 units of insulin did not show any difference in insulin sensitivity between normal individuals and patients with hyperthyrosis. Between cases of more severe and milder hyperthyrosis no essential difference in the sensitiveness to insulin was recognizable. Fixed relations between rise of basal metabolism and insulin sensitiveness are likewise not present.

Preparation of Two Active and Specific Thymus Substances, Their Influence on Calcium and Phosphate Content of Rabbit Serum. — A. Nitschke. (*Zeitschr. ges. exp. Med.*, **65** : 637, 1929.)

The significance and function of the thymus are still very slightly known. Hammar and Gley are in doubt as to the presence of an internal secretory gland. Thomas considers all influence of the thymus on the metabolism as unproved. The author made investigations on rabbits with acetic-aqueous and acetic-alcoholic extracts of thymus. Following one or for the most part two injections a marked fall in blood calcium content occurred with severe tonic-clonic convulsions. The author believes that the fall in calcium is effected by a substance characteristic for the thymus which probably is to be regarded as the internal secretion of the gland. The characteristic symptom in tetany — the electro-hyperexcitability — could also be demonstrated on the animals.

Other experiments with extracts prepared according to definite method, yielded a secre-

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substance likewise with greatest probability specific for the thymus, which lowers the inorganic phosphate of the serum. The calcium lowering principle is water-soluble, acid- and alkali-resistant and resistant to heat. The phosphorus lowering principle is resistant to acid, alkali and heat; it is, however, insoluble in purely aqueous solutions. The thymus must be ascribed a hormonal influence on phosphate metabolism. Important questions are disclosed in this way for pediatrics.

Non-Specific Stimulating Therapy with Insulin and Glucose Forced Feeding Treatment in Chronic Pulmonary Tuberculosis. — H. Bergmann. (*Die med. Welt*, [illegible]: 726, 1929.)

Report concerning 8 cases of tuberculosis treated with insulin. In two cases the treatment had to be prematurely interrupted, since despite careful asepsis at the site of injection, infiltrates originated. On the whole the reports in the literature up to the present, concerning the value of an insulin forced feeding cure in tuberculosis, as well as in severe diseases, which received a careful dosage, are corroborated.

Endocrine Gigantism and Dwarfism. — M. Berliner. (*Zeitschr. ärzt. Fortb.*, **26** : 352, 1929.)

In forms of dwarfism, with exception of chondrodystrophy, very fine results are often to be obtained through the administration of the deficient hormone, especially in myxedema. Perhaps these are to be explained by the fact that under the influence of the hormone administered, the gland itself may be stimulated to renewed effort. In gigantism conditioned by the endocrine glands, the height can be restrained in some cases by ovarian or testis preparations.

Action of Placenta Extracts on pH of the Blood. — Imparato. (*Paris méd.*, **19** : 500, 1929.)

In previous communications the author has shown that intravenous injections of folliculin and pituitary anterior lobe occasion alkalosis whereas corpus luteum and posthypophysary extract cause acidosis. In the present communication it is reported that the results obtained with injection of placenta are uncertain, yet in the majority of cases they occasion alkalosis.

Insulin Treatment of the Fistulae Following Gastric Operations. — A. Lupan. (*Zentrbl. Chir.*, **56** : 1423, 1929.)

In several cases of fistulae of the duodenum, stomach and intestine following gastric resection, injections of insulin were made. The results obtained were very satisfactory since in the shortest possible time a cure of the fistulae and recovery of the patient was attained. The favorable effect of insulin is to be explained by the fact that it is a hormone which activates the basal metabolism of the cell, etc., through marked oxidation of the carbohydrate. The cells get back their vitality whereby a more rapid healing of the wound is obtained.

Report Concerning Results Which Were Obtained with Pituitary Substitution Therapy. — K. Ehrhardt. (*Zeitschr. Geburtsh. u. Gynäkol.*, **95** : 378, 1929.)

In a 61 year old patient with pituitary cachexia the author obtained an increase in weight of 20 pounds, growth of axillary hair and restitution of working capacity within 2 months with pituitary anterior lobe therapy. In other cases Ehrhardt observed fine results from substitution therapy by means of transplantation of anterior lobe of sterilely removed pituitary of cattle in adiposogenital dystrophy and amenorrhea. It was further reported that the pregnancy reaction reported by Zondek and Aschheim was tested in 200 cases and could be entirely corroborated.

Myopathies and Endocrine Disturbances. — On the Subject of a Clinical Observation of Non-Familial Myopathy of the Loeden-Moebius Type with Pluriglandular Symptom Complex. — L. Langeron, R. Caliegue and P. Duquesne. (*J. Méd. Lyon*, **10** : 369, 1929.)

The determination of more or less distinct endocrine disturbances in connection with myopathy in several cases logically led to the trial of an organotherapeutic treatment of the disease. The therapeutic experiment had a very unsatisfactory result. Pituitary, thyroid, thymus, suprarenal, testicular extract and pluriglandular therapy were tried. In the best case a functional improvement was obtained but never a disappearance of the muscular atrophy or a fixation of the atrophic process.

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Concerning the Action of Adrenal Cortex and of Histamin on the Blood Cell Regeneration. — E. Huth. (*Wien. klin. Wochenschr.*, **42** : 739, 1929.)

The author carried out a treatment with adrenal cortex and histamin in more than 60 patients with anemia. Both preparations were found to be of equal value to liver with regard to the regeneration of blood cells. In addition to increase of blood cell count there was regularly shown increased appetite and as a rule also increase in body weight. Four cases of pernicious anemia which had been under liver treatment for weeks in the hospital were changed to treatment with histamin for 3 weeks. The increase of erythrocytes, the improvement of appetite and of the general condition continued as if no change had been made in therapy. Other patients suffering from pernicious anemia received histamin exclusively from the first day of hospital treatment. The results corresponded to that of liver treatment.

Concerning the Morphology of Experimental Hyperthyroidism. The Endocrine System of the Organism in the Act of Growth in Systematic Feeding of Thyroid Substance. — E. Kliwanskaja-Kroll. (*Virchows Arch. path. Anat. u. Physiol. u. klin. Med.*, **272** : 430, 1929.)

In the feeding of rats with thyroid substance the first marked changes in the thyroid appeared after 30 days of feeding. The changes are all the more marked the longer the period of feeding. The cell changes refer to a suppression of gland activity. The hyperthyroidism artificially induced through feeding with desiccated thyroid substance was followed by hypertrophy of the thymus — of its parenchyma. The increase of cortical layer exceeds that of the principal medullary layer. The number of Hassall's bodies is markedly increased in the thymus of the experimental animal. An increase of the thymus may be observed (10 days of feeding with thyroid).

The Alkalin Reserve in Animals Subjected to a Thyroid Treatment. — C. J. Parhon, M. Cahane and J. Orenstein. (*Compte rend. séances soc. biol.*, **101** : 231, 1929.)

The observations relate to 8 full grown dogs who received 2 to 4 gm. desiccated thyroid daily for 27 to 34 days. The hyperthyroidization attained could be demonstrated by the loss in weight of the animals which amounted to 3 to 4 kgm. The alkali reserve was determined according to Van Slyke. In all, 154 determinations were made. From the investigations it is shown that the alkali reserve is lowered in hyperthyroid animals which is manifested in a tendency to acidosis. Saida determined the same diminution of the alkali reserve in clinical observations.

Neuroanemic Syndrome with Optic Atrophy. Failure of Liver Treatment. — J. Dereux. (*Bull. et mém. Soc. méd. Hôp. Paris*, **45** : 577, 1929.)

Whereas several authors, as for example Crouzon, P. Mathieu and Gilbert-Dreyfus, as well as Paul Jacquel and Desbuquois have reported recovery of patients in cases of neuroanemic symptom complex by use of Whipple's method of treatment, the author treated one case in which this therapy failed. It is emphasized that in treatment according to Whipple, it is a question of dissociated treatment. The therapy influences the anemic process but has no influence on the further development of the neurologic process. This observation is not surprising for liver therapy may not get at the basic causes of the disease. P. E. Weil and Picard also have reported concerning this dissociation of action of liver therapy.

Concerning the Hepatic Point of Attack of Insulin. The Primary Paradoxic Insulin Hyperglycemia. — M. Bürger and H. Kramer. (*Zeitschr. ges. exp. Med.*, **65** : 487, 1929.)

The intravenous injection of insulin regularly results in an initial hyperglycemia in man and dogs. The intraportal injection of insulin shows in dogs increase of blood sugar up to 100 per cent, on the average 33 per cent. Following interruption of the liver circulation the primary insulin hyperglycemia remains absent. The primary insulin hyperglycemia is to be obtained with all types of insulin tested. It is a physiological manifestation.

Treatment of Diarrhea Due to Insufficiency of the Digestive Glands. — (*Progrès méd.*, **57** : 969, 1929.)

According to the etiology, treatment must in part be a substitution organotherapy and in part an organotherapy stimulating secretion

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In gastric insufficiency the organotherapeutic measure consists in the administration of natural gastric juices which are prepared under various names and in part in the administration of gastric extracts which contain a hormone (secretin). In pancreas insufficiency it is always to be noticed that pancreas organotherapy acts only in alkalin medium. Pancreas extracts, powder or solution are used. A combination of pancreas with malt can also be given. In manifestations of liver insufficiency, liver preparations in the form of extracts, tablets or fluid extracts come into consideration.

Castration in Pregnancy. — J. Halban. (*Wien. klin. Wochenschr.*, 42 : 697, 1929.)

The corpus luteum has no significance for pregnancy in the human being. Waldstein's investigations show that in pregnancy the placenta produces the ovarian hormone. The fetus does not come into consideration as source of the hormone, since also in cases of cystic mole and stillbirth, the production of hormone is not disturbed.

The Treatment of Arterial Hypertension. — E. Donzelot. (*Le Monde méd.*, **39** : 481, 1929.)

The organotherapeutic treatment of these disease cases can under certain circumstances attain the value of an absolute causal therapy. This is especially the case in organotherapy with ovarian preparations in the course of hypertension of the menopause. Thyroid therapy also, the field of indication of which is extensive, was proposed in small doses (in milligrams and parts of milligrams). This therapy should give encouraging results at times. A substance which deserves much greater interest than those mentioned hitherto is a pancreas preparation. The hypotensive even if not regularly appearing action of this pancreas extract has already been mentioned by various authors; Kisthinios has shown that this pancreas extract can not only cause a fall of blood pressure but can also neutralize the action of adrenalin. Gley and Kisthinios have recently succeeded in showing that the pressure-lowering and blood sugar-lowering action of a given pancreas extract are independent of one another and they have even succeeded in isolating a substance from the pancreas which merely acts by lowering pressure. The injection of this substance makes superfluous a series of precautionary measures which are otherwise necessary, so that a great stride is made in therapy through this. Clinically, it is not yet possible to exactly limit the manner of action and field of action of this special pancreas extract. In any case the administration of this is simple and its use is indicated in particular in those cases of hypertension in which anginous pains appear.

Obesity Through Endocrine and Psychogenic Bulimia. — E. Bonilla. (*Med. Ibera*, **24** : 727, June 1, 1929.)

The patient is a woman of 34 years. Her mother was very fat and so are all the relatives on the maternal side. The patient has always been stout, but not excessively so. Menstruation at 13 years. Flow somewhat scant. Within the last 2 years, amenorrhea for 4 months. She has been married 11 years: had 4 children. Her present illness began during the last pregnancy 1 year ago with great emotionalism, insomnia and sensation of anguish and great hunger. The crises of weakness increased still more after delivery and her great obesity then developed. At the beginning of pregnancy, she weighed 85 kg.; at the present time, 119 kg. Examination of the patient revealed a very great generalized obesity. Basal metabolism was +9 per cent. Mental examination showed that the patient was a marked oligophrenic (torpid imbecile). She was subjected to treatment with thyroidin (4 tablets daily) and restricted diet. Within 2 months, the patient left the clinic with a weight of 124 kg. and a basal metabolism of +9 per cent.

The author believes as does Marañón that every treatment of obesity is mixed; exogenous factors (hyperalimentation, sedentary existence) and endogenous factors (thyroid, neuropituitary, genital, etc.) intervene. Great importance is given to the intervention of the pancreatic factor in the pathogenesis of obesity. The magnificent results obtained with insulin in states of emaciation have changed the conception that insulin insufficiency would cause an excess of carbohydrate to be stored in the organism as fat. Falta maintains that only those individuals can grow fat who possess a normal island function. When this is exaggerated the patients suffer a rapid ontake of fat; but the excess work of the pancreas finally exhausts it, giving rise to prediabetic states and confirmed diabetes. Recently, there have been described

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in the clinic spontaneous hypoglycemic syndromes analogous to those induced by insulin. These syndromes which almost always appear in laborers are characterized above all by crises of great hunger during which the glycemia is very low and which disappear with the administration of food particularly sweets. These crises are induced by a hyperinsulinism. According to Fonseca, hyperinsulinism is constant in obesity. Sometimes it is due to a greater production of insulin and at others to the lack of antagonistic hormones of the pancreas which correspond to thyroid, pituitary and genital obesities; but it is always the insulin which determines the obesity through its fattening effect. This idea alters the one classically admitted concerning the intervention of the genital glands in an identical sense as that of the pancreas in carbohydrate metabolism, based on the greater frequency of diabetes in the climacteric and the facility of inducing spontaneous, alimentary and adrenalin glycemia in castrated animals and women and in the critical age. The changes recently encountered in the pancreas of castrated animals and the hyperglycemic effect of ovarian extracts make one believe that the genital insufficiency induces a hyperinsulinism which causes the obesity. It is very possible that this is so and that the glycosuria of castrated animals and the coincidence of diabetes with the critical age is due to the hyperfunctional reaction of other glands, especially suprarenals which turn the carbohydrate metabolism in the diabetic direction.

All the facts related by the author demonstrate that the insulin hormone plays a primary rôle in those states in which the processes of assimilation are increased. It is more difficult to determine whether there are treatments for obesity whose cause resides in a primary insular activity, either through conditions in the pancreas itself or through an abnormal excitability of the hypothalamic nervous centers, regulating endocrine pancreatic activity. The author's patient appears at first sight to be a typical case of exogenous obesity, induced by excess of food intake consequent to her mental state, although the hereditary antecedents and her slight ovarian insufficiency suggest the existence of predisposing endogenous factors. The great similarity of the clinical picture with the one described by Harris and others, inclines the author to believe in the intervention of a hyperinsulinic factor. In the author's opinion, the fall of the blood sugar curve after ... hours indicates a hyperactivity of the endocrine tissue of the pancreas.

Some Considerations Concerning a Case of Pseudo-Hermaphroditism in a Woman. — S. Recasens. (*Med. Ibera*, 24 724, June 1, 1929.)

The patient presented a peniform clitoris 2 cm. long in flaccidity, and 5 cm. in erection, two swellings resembling testes, one situated on the left labia major, painful to pressure, and the other located in the right inguinal ring. There was an opening in the external genitals at certain distance from the clitoris through which the patient urinated and menstruated. It is a case of pseudo-hermaphroditism because the patient has masculine characteristics. This woman also presented a sarcoma of the ovary. After surgical intervention, it was seen that the sarcoma was located in the ovary with its normal tube. At the same time the two tumors were extirpated. Analysis of these tumors showed that one in the right inguinal passage was a cystic hydrocele; that of the left labia major showed a histological constitution resembling that of an ovarian cyst if on closer examination it does not prove to be a more or less altered masculine genital gland.

Endocrine Rheumatism. — S. Puente Veloso. (*Arch. Med. Cir. y Especialid.*, 30 685, June 8, 1929.)

The author draws attention to the endocrine alterations and the importance they have in many cases of rheumatism. Hyper- hypo- or a-function of the thyroid and ovaries, principally ovary in the female sex, is the determining factor in the rheumatic crisis. These endocrine disturbances in the majority are manifested by trophic disorders, fragility of the nails, vasomotor excitability, tendency to sweating; all depend on thyroid and ovarian dysfunction. In women affected with acute articular rheumatism disorders of the genital tract are often noted, with dysmenorrhea, genital aplasia, with initial menstrual retardation.

Ardillier and especially Leriche have observed the relation between rheumatic pain and ovarian castration. These painful crises, which the author was able to observe, precede the menopause and exacerbate when the menopause occurs and even after the men-

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pause, affecting all the articulations but especially the metacarpo-phalanges and the knees. Sometimes, in patients with rheumatic crises the pains are manifested during the menstrual period after being absent or at least faint before the period. It is interesting to note that women affected with vagosympathetic disequilibrium are most predisposed during the critical age to develop rheumatism. In one patient with a bilateral tuberculous process with rheumatic disturbances, the author was able to follow the evolution of her pain, noting that this exacerbated during the menstrual period and in the 2 months when her period did not appear these crises were of greater intensity, disappearing with thyro-ovarian therapeusis.

Many patients with rheumatism are suffering from thyroid disturbances but in the author's opinion, in the woman, the ovary is the gland which has an intimate relation in many cases to the painful crises. He reports four cases in point.

Antagonism Between the Different Substances in the Pituitary and the Action of Insulin in Normal Dogs and Hypophyseopriva Dogs. — M. A. Magenta. (*La Semana méd.*, **36** : 1275, No. 20, May 16, 1929.)

The oxytocic principle (oxytocin) of the extract of posterior pituitary is the active part in the insulin-pituitary antagonism. The hypertensor principle (vasopressin) does not modify the hypoglycemic action of insulin. An extract of anterior lobe prepared according to technique of Putnam, Teel and Benedict also fails to modify the action of insulin. Oxytocin causes a disappearance of the convulsive symptoms and raises the glycemia of hypophyseopriva dogs in insulin hypoglycemia.

The Antagonism Between the Pituitary and Insulin in Toads. — B. A. H. Houssay and D. Potick. (*La Semana méd.*, **36** : 1275, No. 20, May 16, 1929.)

The injection of insulin into toads 24 hours before injection of extract of posterior lobe of pituitary decreases the action of this extract on absorption; it has little or no effect on the oliguric action of the extract; the two substances dilate the melanophores and their effects are united. Extirpation of the pituitary increases considerably the sensitiveness of the toads to the toxic action of insulin. Extirpation of the anterior lobe only also increases this sensitiveness but in a less degree.

Infundibulo-tuberian lesion does not modify the sensitiveness of toads to insulin. Extract of anterior lobe and of posterior lobe and daily implantation of anterior lobe correct hypersensitiveness of the hypophyseopriva toads. The daily implantation of posterior lobe (intermediate part and nervous) does not produce this effect.

Hypothyroidism Accompanied by Various Neurologic Disorders. — Zygmunt W. Kuligowski. (*Rev. neurol.*, **1** : 514, No. 3, Mar., 1929.)

A female patient of 58 years presented signs of thyroid insufficiency: edema, dryness of the skin, lowering of basal metabolism, flattening of the P and T, waves of the electrocardiogram, slowing of cardiac contractions on radioscopy, increase in amount of albumin in the serum up to 10.25 per cent; diminution of urine, suppression of sweat, chilling, insensibility with regard to vegetative poisons, slowing of movements, slight hebétude. At the same time the patient presents a series of neurologic symptoms of undoubted organic origin.

After treatment with thyroidin for a week, the signs of thyroid insufficiency disappeared; the neurologic signs subsided in part, with the exception of the fixed facies and the absence of Achillean reflexes. The Wassermann test was slightly positive in the blood so thyroid treatment was interrupted to institute specific treatment: it was without effect on the nervous system and the hypothyroid symptoms reappeared. The author believes accordingly that these nervous symptoms are dependent upon the hypothyroidism.

Deviation of the Endocrine Glands as Method of Treatment in Atrophy or Underdevelopment. — J. A. Goljanitzki and A. L. Obolenskaja. (*Arch. klin. Chir.*, **154** : 623, 1929.)

Organotherapy can lead to only one result, when the corresponding brain centers and the vegetative nerves controlled by them can still respond to the stimulus. In centrally conditioned atrophy this therapy proves to be completely powerless. Characteristic for cerebral conditioned atrophies is their polyglandular character and the extensive dis-

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turbance of metabolism. It is clear that organotherapy is condemned to failure in extinguished ability to react on the brain and vegetative nervous system. The attempt to do away with insufficiency of the endocrine glands through a transplantation depends on just as false a presupposition as the "rejuvenation" of these glands through destruction of their excretory portion. On the other hand, there exists the possibility in more or less peripherally conditioned atrophies and aplasias of the endocrine glands to again restore the glands through their reversing to new blood and nerve paths.

The author reports concerning successful interventions in myxedema and in sex gland atrophy.

Concerning the Field of Use of Ovarian Preparations. — Schröder. (*Münch. med. Wochenschr.*, **76** : 84, 1929.)

The ovarian preparations must be tested on well chosen cases. Deficiency symptoms in normal or artificial climacteric are no suitable field. Non-specific preparations also suffice here in addition to those which have always been on the market. Old hormone defects arising secondarily following general disease of the body or directly following pelvic inflammations are not suitable for hormone therapy but only such insufficiencies which may be recognized as obviously located primarily in the ovary.

Interrenal Syndrome. Precocious Menopause, Hirsutism, Virilism, Pseudo-Hermaphroditism. Hypernephroma of the Left Suprarenal Gland. Confirmation of Clinical Diagnosis by Necropsy. Sclerosis of the Thyroid Gland, Climacteric Ovaries. — Syllaba and V. Jedlicka. (*Rev. neurol.*, **1** : 525, No. 3, Mar., 1929.)

The patient was a woman aged 38 years. Normal development of physical and psychic strength during childhood before and after puberty. Married at 29 years, the patient gave birth to two children. At the age of 36 years, menstruation ceased and 1 year later she also lost the orgasm during coitus. At this time she became transformed in external appearance. Her voice became hoarse; her hair crisp, the limit of the hair on her forehead was replaced by appearance of angles of alopecia on the forehead; a mustache developed on her lips and a beard on her chin; the shoulders enlarged. The breasts disappeared and the pubic ha became strong. At the same time the patie became altogether cold in her sexual relatio and even in her maternal love she neglect her children. In the course of the last month terrific pains in the back and in the sacr region. The patient grew weak; she beca bedridden for the past 3 months. In Dece ber, 1928, she had quite a virile appearan in face, head and trunk. The clitoris is 3 c in length, with a duplication of the skin. the left epigastrium there was a tumor a under the tumor the kidney was found. the inguinal region there was a metastasis a in the left pleural cavity a hemorrhagic effu sion.

The author questions whether virilism and hirsutism are due to dysfunction of the supra renal cortex or according to Falta to a hype function. The patient died January 17, 192 and V. Jedlicka presents the microscop preparations. A cortical adenoma compose of young eosinophil cells of large dimension emerged from the left suprarenal, its meta tases into the lymphatic glands and into th left pleura. The right suprarenal was sma with the cortex very much reduced, with th medulla hypertrophic; in the thyroid the was a fibrous sclerosis; in the ovaries a pre cocious climacteric appearance whereas th thymus was completely involuted.

In the discussion M. Pelnai recalls th varied combinations and atypical forms of th interrenal syndrome. There are interesti combinations of beard formation and of vir form of disposition of pelvic hair, that is, triangle. He mentions two similar cases in his clinic, in which this partial masculinis tion appeared at puberty, 1 to 2 years aft the appearance of menstrual periods whi were regular or postponed but always with hyponormal menstruation; the ulterior phy sical and psychic evolution was normal. Th beard appears rather frequently in the meno pause, but it is not known whether it com bines with the virile type of arrangement o hair or whether it is merely a senile hirsu ism. These partial pubertal masculinis tions are certainly not conditioned by simple ovarian hypofunction; it is probab that it is a question of change of interren function but in opposition to the present cas it is a question of temporary pubertal distu bance.

M. Bondy recently examined a singer of years, well developed as a woman; neverth

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less, for some time past a mustache and beard have appeared; menstruation has disappeared and the hair has fallen out and become coarse. There is also a masculine type of arrangement of pelvic hair but no mental change. The most disquieting disorder for a singer is a hoarse voice which accompanied all these changes.

M. Jedlicka has examined several cases of senile beard in women: the suprarenals were always normal and the arrangement of the hair was of feminine type.

Case of Tumor of the Pituitary in a Dwarf. — K. Poncz. (*Rev. neurol.*, **1** : 515, No. 3, Mar., 1929.)

The patient is 34 years old, married. Absence of menstruation for the past 6 years, and of the sexual desire with abnormal obesity. Three years after onset, transient polyuria. For the past 8 months, decrease of vision and headache in the frontoparietal region. Two healthy children, three miscarriages. Parents were of small stature as well as an older sister. The patient under treatment is a dwarf (1.33 m. in height). She is pale, her thyroid is not perceptible. The adipose pannicle is very much developed. Percussion of the forehead is painful. Examination of the fundus of the eye shows slight atrophy of the right optic nerve. Visual acuity on the left: 1/24. On the right, 1/60. Bitemporal hemianopsia. Arterial tension 9 to 5. The ovaries are small; the mammary glands but slightly developed; there is no axillary hair, but little on the pubis. The radiograph of the skull shows an enlargement of the bottom of the sella turcica, the back and posterior clinoid apophyses are injured. A diagnosis of tumor of the pituitary was made. Despite radiotherapy, the vision became more disturbed; at the present time the right eye no longer sees anything and the left only what is before it. In addition to the tumor, the patient presents an evident dwarfism (infantile dwarfism of Pal-tauf). In its evolution Dr. Bregman distinguishes three stages: (1) The child develops at the expense of the potential cellular energy which brings growth up to a certain stage; (2) during a second period insufficiency of the endocrine glands becomes evident, in particular of the anterior lobe of the pituitary, which in normal conditions excites the ulterior development of the cells. The consequence is arrest to a dwarf height. With time this hypofunction is expressed by still other phenomena (suppression of menstruation and disappearance of sexual appetite); (3) finally, in a third period, a tumor of the pituitary made its appearance which took on a malignant character (benign formerly; probably teratoma) and led to loss of sight.

Relations Between the Pituitary and the Testicle. — B. A. Houssay and J. M. Lascano Gonzalez (*La Semana méd.*, **36** : 1275, No. 20, May 16, 1929.)

Toads deprived of their pituitary present a very appreciable testicular atrophy at the month of operation. The testicles weigh less and there is marked atrophy of the spermatogenetic epithelium; the spermatozoids already formed persist. When only the anterior lobe is extirpated a similar atrophy is observed but less marked. In the craneotomized toads or in those with lesions in the infundibulum there is no testicular atrophy. Subcutaneous implantation of the pituitary increases the size and weight of the testicles of craneotomized toads beyond that of controls. Implantation not only impedes the atrophy in the toads deprived of pituitary but increases in size above the normal; the tubes are dilated with fluid; the activity of the spermatogenic elements is exaggerated. In some toads precocious sexual maturity is observed.

The Functions of the Pituitary and the Infundibulo-Tuberian Region in the Toad Bufo marinus (L.) Schneid.—B. A. Houssay and L. Giusti. (*La Semana méd.*, **36** : 1275, No. 20, May 16, 1929.)

The authors complete the studies on the question begun by one of them in 1910 and continued since then. The present communication is based on the observation of almost a thousand toads during the years 1927, 1928 and 1929. In this species it is possible to distinguish perfectly the symptoms corresponding to each one of the portions of the gland and to lesion of the infundibulum. The entire pituitary has been extirpated or only the glandular lobule; the tuber has been cauterized and in others only a simple craneotomy has been performed. The counterproof has been effected by means of injections of extract, grafting or repeated implantation of the distinct portions. Glandular insufficiency produces the following symptoms. Pallor of the skin by retraction of the melanophores (insufficiency of the intermediate part); tes-

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ticular atrophy; asthenia and convulsions (which certainly are not specific); high mortality; hypersensitiveness to insulin. The first symptom is very specific; the others are very intense in those deprived of pituitary, somewhat less in those deprived of the glandular lobule. These symptoms are missing in the craneotomized or those with lesions of the infundibulum. The repeated implantations, the grafting and the injections of extracts correct these symptoms. The glandular hyperfunction is revealed by darkening of the skin. The infundibular symptoms are the following. Formation of a cutaneous pellicle (trophic disturbances and ulcerations of the skin) abortion and polyuria. These symptoms are observed in toads deprived of pituitary or of glandular lobe, in the majority of those with infundibular lesions and in some with other brain lesions.

Nervous Lesions Found at Autopsy in a Subject Affected with Adiposogenital Syndrome. — L. Babonneix and J. Lhermitte. (*Rev. neurol.*, 1:495, No. 3, Mar., 1929.)

Eight years ago one of the authors presented the case of a man of 47 years in whom symptoms of four types had been noted. (1) hydrocephalus of long standing with optic atrophy, blindness and headache. (2) Hydromyelia or syringomyelia: preacher's hands, atrophy of the muscles of the hands and forearms, cervicodorsal kyphosis, abolition of tendinous reflexes to the upper members, exaggeration of the same reflexes in the lower members. (3) Adiposogenital syndrome: obesity (82 kg. for 1.58 meters height); presence of lipomatous masses in various parts of the body, testicular agenesis, gynecomastia, almost complete lack of sexual desire. (4) Polyuria.

After discussing these symptoms which appeared following repeated meningeal reactions, the first of which dated back to the sixth year, the authors conclude that it was doubtless a case of hydrocephalus with hydromyelia which had determined the production of an infundibular syndrome.

Recently the authors were able to examine the nervous system of this subject who had succumbed to a new attack of meningitis. They found very marked hydrocephalus with large dilatation of the third ventricle and atrophy of its walls, especially lower and anterior; (2) hydromyelia of the cervical marrow.

Despite the absence of all information concerning the pituitary, these observations show the importance of tuberian lesions in the production of the adiposogenital syndrome, the anatomic cause of which is so disputed; they confirm once more the existence of an infundibular polyuria. The hydromyelia accounts for the atrophy of the upper members.

Recent Facts Concerning Hormones. — U. Ebbecke. (*Dermatol. Zeitschr.*, 55 : 177, 1929.)

The secretin of the intestinal mucosa which stimulates the secretion of the pancreas reaches the circulation through the hydrochloric acid of the stomach when it is excreted from the intestinal epithelium which contains it in absorption. Acetyl cholin was referred to by Le Heux as hormone of intestinal peristalsis. The sympathicomimetic adrenalin is a typical nerve hormone. Thyroid hormone increases the excitability of the vegetative nerves and in the pituitary the relation is so intimate that it is disputable up to the present which of the symptoms is to be ascribed to the pituitary itself and which to the neighboring vegetative centers of the midbrain. There is no hormone gland which does not stand in relation to the sex glands and that holds true for the endocrine glands in general. All stand in interrelationship to each other. The hormone glands are to be conceived as a complex regulating organ function. The hormone glands influence the affective and psychic life. On the other hand the hormone glands are dependent on the secretory nerves.

Ismar Boas

(*Continued from page 83*)

excellent pedagogy and high inspiration, won the admiration and gratitude of all.

An autobiography, published in Volume VII of *Medizin der Gegenwart*, furnishes interesting and intimate details of Boas' life and at the conclusion of this article there is a comprehensive list of his writings. The individual articles amount to well over a hundred. A textbook concerning the therapy and diagnosis of diseases of the stomach has been so universally accepted that the ninth German edition has appeared. It has also been translated into English, Italian, Span-

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and Russian. Two volumes, as a sequel to this, concern the therapy and diagnosis of diseases of the intestines, and have had two editions. The collected works of the twenty years of experience at the Boas *Privatpolyklinic* (the direction of this clinic was given over into the hands of Prof. Boas' able assistant, Dr. H. Elsner, in 1906) is published in two volumes.

Some of the special problems which have been treated by Prof. Boas are the following: Gastritis acida, occult hemorrhages, gastrogenous diarrhea, deep duodenal stenosis, enteritis membranacea, hypertrophic pylorus stenosis and its treatment, colitis ulcerosa, hemorrhoides, balneotherapeutic treatment of gastro-intestinal diseases, and other therapeutic methods. For the *Verein für innere Medizin*, in Berlin, 1900, Boas reported on the subject of carcinoma of the large intestine; for the Paris Congress in the same year, where he presided over an autopsy of the intestinal tract, he reported on enteritis membranacea. Further honors were accorded him at practically every meeting or society for the study of gastro-enterology. A report on "Chronic Appendicitis" for the Symposium on Gastro-Enterology, was published in English in the *Medical Journal and Record* (January 6, 1926). As Boas states, the report "gives not much new" but it is a careful survey of the present opinions on appendicitis, and it contains several helpful suggestions in the diagnosis of appendicitis. "Even if the diagnosis may be doubtful — of course not in typhlophobia — I am in favor of operation, particularly in children and young adults." With this statement Boas takes a definite stand on the subject of appendicitis, and for the uncertainties that still exist concerning the nature of appendicitis, he hopes that "the intelligent cooperation of surgery and internal medicine will endeavor to straighten out the difficulties." "Habitual Constipation," 1923 (translated into English by Dr. Thomas L. Stedman), has been popular, mainly for the reason stated by the author, "It is intended in no way to supplant the physician, but to second his efforts toward effecting a cure for this widespread evil through judicious counsel." The book contains sensible advice, "in non-technical terms," some unusual opinions suggestive of Coué and among other things, several special diets. In the work on diets, which was an outgrowth of the study of digestion, Boas has been both practical and thorough. It is reported that the students in his clinic were not only taught what food to prepare but also, how to prepare it, and they were required to attend classes in cooking in conjunction with their medical studies.

As a prolific scientific writer, a profound investigator, a wise counsellor and an interesting person, Boas offers a striking example of one who is not only putting a great deal into life, but is also getting a great deal out of it. He has well earned his world fame, for his work is all of the highest type and has proved universally acceptable.

The Clinical Fields of Use of the Sexual Hormone Preparations (Their Clinical Test). — R. Schröder. (*Deut. med. Wochenschr.*, **55** : 3, 1929.)

Sexual preparations well tested biologically must first pass the test of their clinical usefulness. This must be undertaken critically and also energetically if practical results are desired from the valuable theoretical biological results of this type of research. As clinical test for the hormone preparations, cases are first of all to be considered suitable in which it is a question of a moderate deficiency of ovarian hormone without other disease manifestations in the body. As clinical test analogous to the growth test in animals, there is stimulation of turgor and growth of a contracted uterus and analogous to the estrous reaction there is the time regulation of the appearance of menstruation, therefore, of the cycle tempo. On the other hand, increased menstruation or prolonged hemorrhages dependent upon abnormal processes are not suitable. These are dependent upon so many, almost always local factors of the genital tract and have not the slightest connection with the ovarian function. The use of test preparations is unnecessary in the so-called deficiency symptoms.

The question of dosage is still completely unanswered; everything is provisionally given over to the individual trial. At this time the proposal of Laqueur with his Dutch colleagues, which has just appeared in the Dutch Obstetrical Journal, is very opportune. This dosage rests on experimentation for a suitable distribution, increase of dosage and sudden cessation. It is connected throughout to the theoretical conception expounded by the author concerning the origin of the hemorrhage. Not that in any way a successful result is to be prophesied herewith, since we do not know whether the relation of sub-

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cutaneous to oral dosage is correct, or whether the absolute amount is sufficient. It is, however, possible that with this beginning we can compare the results of the different observations and make new conclusions on these bases. Patience is essential for success.

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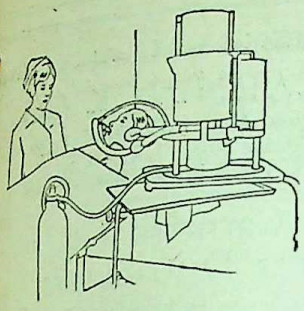
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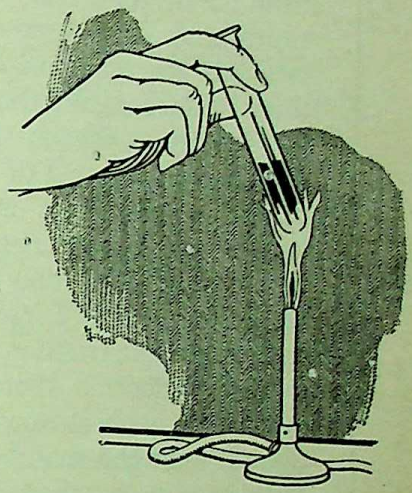
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is desirable in all cases and imperative in grave cases of

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Abstracts (Continued)

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Concerning the Various Actions of Histamin and Adrenalin on the Blood Vessels in the Rabbit's Ear

Circulatory Problems

Therapeutic Application of the Hormone of the Circulation

Embolism and Thrombosis

Concerning the Relationship of Pituitary Gland and Hypothalamus to the Retention of Water

Folliculin, Insulin and Diabetes

The Basal Metabolism

Relations between the Digestive Tract and Blood Diseases

The Internal Secretion of the Salivary Glands

Endocrinology and Opotherapy

Skin and Venereal Diseases

Concerning the Rôle of Adrenalin, of Insulin and Glycogen Sugar on the Mechanism of Attacks of Angina Pectoris

Concerning the Action of Post-Pituitary Extract on the Musculature of the Uterus

Concerning the Influence of Administration of Thyroid Gland on Albumin and Fat Metabolism

The True Acidity in Isolated Portions of the Male Genital Apparatus of the Rat and Its Hormone Limitation

Transplantation of Preserved Ovary. IV. Transplantation of Desiccated Ovary

Investigations on the Origin of Creatin or Creatinin in the Animal Organism

Experimental Investigations on Corpus Luteum

Hormone of the Anterior Lobe of Pituitary as Related to the Male Genital Tract

The Zondek-Aschheim Pregnancy Reaction

Organ Extracts in Their Action on Immuno-Biological Processes

Insulin and Nutrition Depots

(*Continued on page 187*)

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Insulin, Epinephrin and Sugar Metabolism

INSULIN and epinephrin are important factors in carbohydrate metabolism. Their action is opposed and is exerted in the peripheral tissues. Epinephrin increases deposition of liver glycogen, insulin decreases it.

In considering the sugar metabolism of the body, the oxidations which give rise to the energy supply and the manner in which the nutritive material is stored and released for oxidation, the logical starting point is glycogen. Glycogen is a polysaccharid — a storage sugar — and is found in almost all the tissues of the body, but particularly in the liver and muscles. Glycogen is one of the products synthesized in the body, principally from the carbohydrates but also from the proteins and the products of protein cleavage — the amino acids (1). Whether fat may be converted into glycogen is still debatable.

Under ordinary physiological conditions carbohydrate metabolism is characterized by continuous activity in both muscles and liver. As soon as the dextrose of the blood reaches a low level due to oxidation by the cells the deficit is made good by the glycogen of the liver, which, under the influence of the enzymes of the hepatic cells, undergoes transformation into blood sugar (dextrose). The glycogen of the muscles is converted into liver glycogen by a process which has received considerable attention recently and which is now fairly well understood.

Since it was clearly evident that injection of epinephrin gave rise to hyperglycemia and

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glycosuria, and since the greatest sugar values were obtained in animals rich in liver glycogen, it was assumed by early workers in the field that epinephrin reduces the glycogen store of the liver. Evidence began to accumulate, however, that epinephrin may actually cause a formation of glycogen which is deposited in the liver. Pollak (2) found that in starved animals as much glycogen may be formed by injecting epinephrin as by carbohydrate feeding. Kuriyama (3) also reported increase of liver glycogen following epinephrin injection.

J. Markowitz (4) found that "The injection of epinephrin into starved rabbits always evokes extensive hyperglycemia, even when the injections are kept up for days.

"When the liver is glycogen-free, injection of epinephrin does not lead to hyperglycemia. When the liver contains traces of glycogen, hyperglycemia of delayed onset ensues, the extent being proportional to the amount of glycogen.

"Mere starvation does not make rabbits glycogen-free. Starvation in the cold, followed by strychnine convulsions will make the liver, heart and muscles glycogen-free for several hours.

"Repeated injection of epinephrin into starved, strychnine-treated rabbits permits glycogen to accumulate in the liver, heart and muscles.

"When insulin is given to starved strychnine-treated rabbits along with epinephrin, considerable quantities of glycogen, up to 2.77 per cent accumulate in the liver.

"The above experiments together with those quoted from the literature, demonstrate that glycogen is obligatory, and not an optional step in the formation of blood sugar from the non-carbohydrate stores of the organism."

C. F. and G. T. Cori (5) investigated the whole problem of glycogen formation and the effect of both epinephrin and insulin on glycogen and blood sugar. The earlier views of the action of epinephrin assumed a direct action on the glycogen of the liver. Actual little investigation appears to have been ma on this point. Since the source of blo sugar was known to be the glycogen of the liv it was assumed rather than observed that t increase of blood sugar and glycosuria f lowing epinephrin injection was due to an a tion in converting liver glycogen into dextro

In Coris' work the assumption was ma of an extra-hepatic point of action. Insul and epinephrin exert opposed actions o blood sugar. Insulin acts by causing mobilization of liver glycogen and there a no differences in rate of disappearance of liver glycogen in normal and adrenalectomize animals following insulin injection. Actual the site of epinephrin action was found to b on the glycogen of the muscles rather tha that of the liver. The earlier observation of an increase instead of a decrease of liv glycogen were confirmed. Epinephrin con verts muscle glycogen first into lactic ac which is then converted into liver glycoge which therefore increases in amount.

In order to ascertain whether liver glycoge can be formed from lactic acid, δ-lactic acid its sodium salt and γ-sodium lactate was fe to fasting rabbits with a resulting deposit glycogen in the liver. This was consonan also with previous work which showed a marked increase of lactic acid in the blo following epinephrin injections. The po sibility that epinephrin causes an increase liver glycogen by conversion of protein glycogen is dismissed as having less evidenc to support it. In the discussion of one their papers the Coris say:

"According to the generally accepted exp nation epinephrine causes hyperglycemia, a after large doses, glycosuria, merely becau it mobilizes liver glycogen. As pointed o in the introduction, hyperglycemia and gl cosuria can not be explained on this basi because there is not enough liver glycoge present to provide the tissues for hours wi sugar at a rate which is greater than th normal ability to utilize sugar. This is ill

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rated by the following calculation. In the experiments in Table IV the average blood sugar was 174 mg. per cent 3 hours after the epinephrine injection. In order to produce a hyperglycemia of this magnitude in normal rats, glucose must be infused intravenously at a rate of 250 mg. per 100 mg. of body weight per hour (Cori and Cori, *J. Biol. Chem.*, 1927, lxxii, 597). Hence, a mobilization of 750 mg. of liver glycogen or an initial glycogen content of the liver of 20 per cent is required, if the hyperglycemia of 174 per cent is to be explained merely on the basis of glycogen mobilization in the liver. Actually there were only 218 mg. or 5.6 per cent liver glycogen present to start with (Table II), and the liver glycogen showed an increase after the epinephrine injection. This indicates that other factors play a rôle in the production of hyperglycemia besides mobilization of liver glycogen. In fact the experiments with epinephrine in Table IV, when taken at their face value, give no evidence that liver glycogen is being mobilized; only by means of a finer analysis could it be shown that mobilization of liver glycogen occurs.

"Decreased utilization of blood sugar is one of the principal causes for the epinephrine hyperglycemia under postabsorptive conditions. The blood sugar rises after epinephrine injections, because the utilization of blood sugar in the peripheral tissues falls behind the supply of blood sugar by the liver, even if the supply is not much higher than normal. For this reason, amounts of sugar given off by the liver will cause hyperglycemia, amounts, which when injected into normal animals, have no effect whatever on the blood sugar level. Hitherto it has been assumed that a decreased utilization of blood sugar must be associated with a decreased carbohydrate oxidation. The present experiments reveal that after epinephrine injections carbohydrate oxidation is carried on at the expense of muscle glycogen and that the carbohydrate oxidation may be increased in spite of a diminished blood sugar utilization."

"The conversion of lactic acid derived from muscle glycogen into liver glycogen explains why epinephrine hyperglycemia can persist for several hours without causing depletion of the glycogen stores of the liver. A decrease in liver glycogen is to be expected only if glycosuria develops. In rabbits during epinephrine glycosuria more sugar appears in the urine than can be accounted for by the disappearance of liver glycogen, indicating that resynthesis of liver glycogen from lactic acid occurs also in this species (unpublished experiments). It can now be understood why different observers obtained conflicting results when they determined the glycogen content of the liver after epinephrine injections. With small doses of epinephrine, or even with large doses when the glycogen content of the liver is low, resynthesis of liver glycogen from lactic acid exceeds mobilization, and consequently the liver glycogen is found higher after the injection. With large doses and a high liver glycogen the latter diminishes because the loss of sugar in the urine can not entirely be compensated by resynthesis of liver glycogen.

"It is surprising that an extrahepatic action of epinephrine on carbohydrate metabolism has not been emphasized before. The experiments on 24 hour fasting and on rats in the postabsorptive state indicate that the extrahepatic action of epinephrine consists in a mobilization of muscle glycogen. Whether this mobilization is responsible for the decreased utilization of blood sugar, or whether both processes are influenced independently by epinephrine, can not be decided at present.

"Since the end-product of glycogen breakdown in the muscle is lactic acid, epinephrine can not raise the blood sugar level after removal of the liver. However, the influence of epinephrine on blood sugar utilization is demonstrable on hepatectomized animals, as will be shown in subsequent papers.

"Insulin produces hypoglycemia because the supply of sugar falls behind blood sugar

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utilization, in spite of a rapid mobilization of liver glycogen. Epinephrine and insulin antagonize each other on account of their opposite effect on blood sugar utilization in the peripheral tissues."

The experimental work showed that in control rats 216 mg. of glycogen disappeared in 3 hours time: 23 per cent was derived from the liver, 77 per cent from the rest of the body.

In animals injected with epinephrin all the glycogen which disappeared was derived from the body, the glycogen of the liver being actually increased. After insulin, 43 per cent of the disappearing glycogen was derived from the liver and 57 per cent from the body. The differences in carbohydrate oxidation were extreme and point to the great differences in action on carbohydrate of epinephrin and insulin. In comparison with the controls, epinephrin injection caused an increase in carbohydrate oxidation of 19.5 per cent and insulin, 97.3 per cent.

The so-called antagonistic effects of epinephrin and insulin on sugar metabolism are, in the light of the Coris' work, not antagonistic in the sense that one opposes the action of the other, for it will be shown later in this article that insulin very likely counteracts the action of epinephrin by synthesizing the precursor of glycogen which epinephrin breaks down. Cori and Cori, however, state that, "Whether or not these two hormones act antagonistically by influencing the same process in an opposite direction must remain undecided as long as the actual point of attack on the carbohydrate molecule is unknown. . . . ." "Insulin is the hormone that leads to a preferential utilization of blood sugar and indirectly of liver glycogen. The antagonistic action between insulin and epinephrine is explained by their divergent effect in blood sugar utilization."

Macleod (6) had predicted the same thing without the experimental facts later demonstrated. "Although in their effects on blood sugar, the two hormones may therefore be said to be antagonistic, it must be remembered that this may be of little physiological significance, and merely be due to the fact that insulin leads to the disappearance from the blood of the excess of glucose which epinephrin causes to be liberated from the liver just as it does when the excess of glucose is absorbed from the intestine, or administered parenterally."

It has now been shown that epinephrin actually acts on muscle glycogen and that the increase in the blood sugar is due to the formation of liver glycogen from the lactic acid derived from muscle glycogen. Blood sugar rises because the increased liver glycogen gives some additional sugar to the blood and this accumulates due to a depression of utilization by the peripheral tissues. The blood sugar is again available for use in oxidations and in storage of glycogen in the muscles and the cycle is complete.

This "cycle of carbohydrates" with lactic acid in the intermediary stage is based upon some of the soundest physiological research. A. V. Hill (7) has outlined series of changes taking place in muscle which his own researches and those of Meyerhoff and Fletcher and Hopkins have established. These changes studied in the complete absence of oxygen are as follows:

"(A) Glycogen disappears.

"(B) Lactic acid appears in equivalent amount.

"(C) Preformed CO_2 is driven off.

"(D) Heat is produced proportional to the lactic acid formed.

"(E) The hydrogen ion concentration rises."

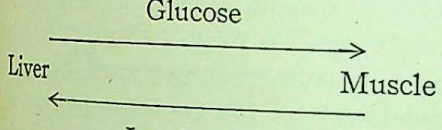
The part played by the lactic acid has been described. Hill says that in the period of recovery (following the anaerobic phase above) oxygen must be taken in to provide the necessary energy. He describes the two phases in the recovery process. The first is the oxidative removal of lactic acid in the muscles where it was formed, and the second is the removal of lactic acid which has

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time to escape by diffusion into the blood. It is this part which escapes oxidation (with the consequent liberation of energy) that Cori and Cori describe as the precursor of liver glycogen and a link in the "carbohydrate cycle." These findings (in so far as epinephrin causes a decrease in muscle glycogen and an increase in liver glycogen) have recently been corroborated by Blatherwick and Sahyun (8) and by Himwich, Koskoff and Nahum (9) who also demonstrated the part played by lactic acid.

"The glucose and lactic acid content of the blood of twenty-nine amytalized and eleven decerebrate dogs was studied during rest and exercise. As indicated in the schema, a glucose-lactic acid cycle exists between muscle and liver. Lactic acid liberated from muscle finds its way to the liver through the blood stream, and is there converted to carbohydrate. The liver in turn yields glucose to the blood, thus affording a supply of carbohydrate to muscle.



It must therefore become apparent that by virtue of this cycle, the liver becomes an integral part of the mechanism of recovery."

The part played by insulin seems in most respects opposed to that of epinephrin. Insulin acts by utilization of liver glycogen instead of muscle glycogen. It increases the peripheral oxidation of blood sugar as well as converts it into an unknown storage substance. In bringing about these effects it causes the withdrawal of liver glycogen which is converted into blood sugar. Liver glycogen is the only source of blood sugar and insulin acts both in the phase of liberation of glycogen and in the phase of utilization of the liberated dextrose.

In considering the action of insulin it becomes more apparent that glycogen is not a mere storage form of sugar but is in all probability an indispensable intermediary stage in the final utilization of carbohydrate in the body. Irrespective of its origin either from carbohydrate or protein (or possibly fats), it must finally be deposited in the liver to be available for formation of blood sugar. It has been suggested that this may be a necessary step because the dextrose which is formed from liver glycogen may be of a different type from the α-β-dextrose from which it is synthesized. In view of the unavailability of muscle glycogen it is possible that the glycogen synthesized in the liver is also of a different type than muscle glycogen. Glycogen is not well understood in its chemical characteristics. The evidence of a special form of "active" dextrose differing from α-β-glucose, which may be necessary before it can be oxidized by the body has been given in previous issues of the JOURNAL. Insulin may either be necessary for the formation of this special type of dextrose which can then be oxidized by the tissues, or it may require it, and no other type, in order to effect the oxidation. Another possibility may be suggested. Insulin may be necessary for the formation of a special type of glucose capable of being synthesized into the unknown substance (hexose phosphate?) which is a precursor of glycogen. The mechanism of action of insulin, however, on glycogen formation and sugar utilization is not understood. In diabetic animals insulin injections cause a disappearance of sugar from the blood by increased oxidation and an increased formation of glycogen. In normal (starved) animals, however, insulin inhibits glycogen storage, and in normal well fed animals it reduces glycogen. Macleod says that in normal animals the amount of free glucose in the tissues (tension of glucose) is reduced and sugar disappears from the blood: this disappearance is not due to a polymerization of glucose to glycogen or entirely to an increase in the relative amount of carbohydrate undergoing combustion. Macleod terms the condition which permits the relatively

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enormous removal of sugar from the blood, a "sugar vacuum" of the tissues. Experimental evidence is against the conclusion that the sugar disappears as a result of some sort of glycolysis in the blood itself, whereby the blood simply holds the products of sugar hydrolysis. Actually the experiments showed that the site of insulin action is in the cardiac and skeletal muscles and not in the liver. Since in normal animals the removal of sugar by insulin can not be accounted for by increased formation of glycogen or entirely by increased oxidation, the problem becomes one of accounting for the fate of the sugar. Macleod (9) accounts for it as follows:

"We believe by assuming that insulin stimulates the formation of some unknown substance which maintains a certain equilibrium with glycogen, and stands on the way between this and lactic acid. This unknown substance may be a stepping stone in the conversion of carbohydrates into fats, and it is possible that in its formation a phosphorous acid complex, such as hexose phosphate is involved."

In addition to this storage of blood sugar as glycogen or as an unidentified precursor of glycogen, there is an increased oxidation of carbohydrate following insulin injection. This is shown by an increased respiratory quotient and by an increased oxygen consumption. The extent to which it is oxidized, however, can not account for all the sugar leaving the blood. In diabetic animals the action of insulin is to definitely increase the oxidation of carbohydrates.

The possibility of some endocrine substance or substances secreted by the pancreas, other than insulin which might exert an influence on carbohydrate metabolism has long been a subject of speculation. Many experiments and clinical observations strongly suggest it. N. F. Fisher (10) reached the conclusion that "Insulin probably does not represent the entire pancreas hormone complex, since in the total absence of the pancreas insulin can not maintain life or does not control all the diabetic symptoms (subnorm... weight, polyphagia, polyuria)."

Chaikoff, Macleod and Markowitz (1... found that when insulin injections were su... plemented by daily feeding with raw pa... creas, dogs could be maintained in go... bodily nutrition and concluded:

"That the presence of something derive... from the pancreas either its digestive fe... ments or some internal secretion beside... insulin is necessary for the maintenance ... normal metabolism."

Recently, Ronzoni, Glaser and Barr (12... have demonstrated the presence in the pan... creas of a substance which exerts an inhibitor... effect on glycolysis in muscle. They al... arrive at the conclusion that a hexose pho... phate (see Macleod's assumption above) ... a necessary part of lactic acid formation ... muscle. "In muscle extracts then the or... mechanism by which lactic acid is produc... is through the intermediary involving carb... hydrate and phosphate disappearance, pr... sumably hexosephosphate. Unless the mec... anism existing in muscle, frozen and hash... is different from that in muscle extract, th... is evidence that the preformed precursor ... lactic acid existing in muscle is a comple... involving carbohydrate and phosphate." Th... work suggests that (at least in solution ... muscle extracts) carbohydrate combines wi... phosphate to form hexose phosphate ... this compound is then broken down into la... tic acid and phosphate. The inhibitor e... ment of the pancreas acts on the phase ... phosphate-carbohydrate formation — inhibi... ing the process of esterification and preventi... an accumulation of this precursor of lac... acid. The subsequent breakdown of th... ester (hexose phosphate) into phosphate a... lactic acid is not materially affected by th... inhibiting substance.

The knowledge of the opposed effects o... pancreas internal secretion and epinephrin... on blood sugar has been largely extended ... The following facts have apparently be... demonstrated. Both exert their action in ...

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peripheral tissues and not in the liver or on sugar in the blood. Insulin apparently stimulates the production of an ester or some unknown substance (probably hexose phosphate) and a pancreatic inhibitor substance retards it. This substance (hexose phosphate?) is a precursor of glycogen and doubtless stands in chemical equilibrium with it. A pancreatic inhibitor substance exerts an opposed effect and inhibits the synthesis of hexose phosphate. Epinephrin increases the mobilization (oxidation) of muscle glycogen and decreases the utilization by the muscles of blood sugar. The products of muscle glycogen splitting (lactic acid) are synthesized into liver glycogen.

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A Contribution to Kottmann's Reaction

(Translated from the article by Dr. Emil Walder, *Mitt. Grenzgeb. Med. u. Chir.*, 1926, 39 : 626, No. 4/5.)

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(CONTINUED FROM VOL. XIV, No. 2)

III. *Concluding Remarks*

In the work given before we have regarded the Kottmann reaction perhaps too much from the standpoint of pure colloid chemistry; in this we are, however, convinced that the colloid chemist himself would have proceeded still more critically. We drew attention to positive sources of error of the method and showed that the opinion of Kottmann that the degree of browning of his sera is a direct measure for its degree of dispersion or its dispersibility is not yet demonstrated, which moreover Prof. Kottmann acquiesced in an oral discussion. We showed that the relations between degree of dispersion and degree of browning are not of so simple a nature, and demonstrated in concrete examples, as Kottmann himself also says, that "profound investigations are still necessary to clear up the theoretical basis of the method in all directions" or, as it is reported later, "that without doubt the method is still further to be cleared up and in need of development in various points".

If we review the literature which has appeared concerning the Kottmann reaction, we must observe that certain authors who work with the method, perceive in it, as it were, a dispersometer for serum and in part on the basis of their results with the Kottmann reaction produced theories concerning physiology and pathology of the thyroid

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function, which, it appears to us, go somewhat too far. So, for example, says F. Starlinger ("Physico-Chemical Investigations on the Thyroid Problem," *Grenzgeb.*, Bd. 36): "And finally Kottmann offered his photoreaction, which properly first conceived the physical condition of the albumin colloid in the serum, so to speak, bodily . . .." That this physical conception of the albumin substance is still problematic we believe we have shown sufficiently. We do not wish to enter into this point, but permit ourselves several remarks on another declaration of Starlinger. In the same work, Starlinger says, in part on the basis of his results with the Kottmann reaction, that a task of the thyroid is to transform coarsely disperse albumin into finely disperse. A struma which does this is said to be hyperfunctional; on the other hand, the reverse is also said to occur, that, to be sure less frequently, the finely disperse serum appearing in the thyroid leaves it as coarsely disperse, "lowering of the plasma dispersion in venous blood characterizes the hypofunctioning goiter." A positive contradiction appears to us to be present here. A gland, which reverses its function on the contrary — which was the case in the hypofunctional struma, according to what was said above — does not seem to us to be hyperfunctional; in our opinion, it should rather be called "contrafunctional." That in general a gland can reverse its function to the opposite, seems explainable with difficulty. It is well known that there are ferments which reverse their effect from a certain concentration of the reaction product. That, however, a whole gland reverses its activity, falls out of the bounds of what is known up to the present. A gland can show hyper-, dys- or hypofunction. We do not, however, as yet know "contrafunction." If the normal or hyperfunctioning thyroid truly displays a dispersing activity for the serum, it must be assumed that the diseased, hypofunctioning gland does this in lessened measure or no longer at all. The border case would therefore be that in which the gland simply allows the blood to pass through changed, so that the entering and leaving plasma shows the same dispersion. One could only arrive at the Starlinger conception if one would make the auxiliary hypothesis that the dispersion would be coarsened by passage through any indifferent organ. Points of support for such an assumption are however not known to us. The difficulty with the whole thing must lie elsewhere. Before we can proceed with the solution of such questions, we must have at our disposal methods which permit us to compare the degree of dispersion of the various sera or plasma, measured in absolute proportion, free from objection. This is, however, not yet the case. Aside from this we do not in general know how the physical process of change of dispersion stands in respect to the chemical decomposition of the albumin molecule which seems to stand in the foreground in thyroid function. Increase in dispersion proves no albumin decomposition as yet although it can precede it. It is self evident that nothing is changed in the fundamental question of an internal secretory process in the thyroid through these discussions concerning the dispersion.

As far as the method is concerned, Starlinger also says that the values of the Kottmann reaction are of course to be realized with some precaution, since precisely with this method the individual shades of color present a rightly subjective factor. He prevents the coagulation of the blood through the addition of citrate, in order to be able to determine the dispersion of the plasma; now we have already cited at the beginning of our work the changes in color observed by Lüppo-Cramer in the growth of gelatin-containing silver germs under the influence of phosphate or citrate. The possibility is suggested that also in the colloid silver arising according to Kottmann, the color changes may appear under the influence of citrate. One would accordingly first have to test the influence

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of the citrate experimentally. Whether the citrate is without influence on the dispersion of plasma we also do not know.

Still another brief remark on Starlinger's work. He says that the cubital vein blood serum on which the whole organism has finished working can not give any more enlightenment concerning the function of the thyroid. Of course, the thyroid secretion is very quickly changed in the living blood or organism as the most recent investigations show. The investigations of Hara and Branovacky show, however, that in pronounced functional disturbances it still remains biologically active. Our own investigations show the same thing. In our tables we also compare with each other venous blood sera from the arm in normal, exophthalmic goiter patients and cretins, in order to determine that in exophthalmic goiter the delay in reaction is definite and the degree of browning is a little less intensive. Moreover, Kottmann's investigations show this already, and he performed his reactions only with venous blood from the arm.

Another author, E. O. Schmidt ("Concerning Morbus Basedowi," *Grenzgeb.*, Bd. 33, 1921) used for the performance of the Kottmann reaction 5 per cent instead of 0.5 per cent solutions of potassium iodide and silver nitrate, subjected it to light with 200 candles for 10 to 25 minutes — at what distance he does not say. In this tenfold stronger concentration of the reagent probably the albuminous substances of the serum, in their function of dispersing agent, result in the ensuing colloidal silver iodide, and the silver is so strong in the background that quite possibly one sees a reaction totally differing from the Kottmann reaction. In so strong a concentration it is possible that most of the silver iodide formed does not remain as a colloidal solution, but instead precipitates out directly. Moreover, we have also referred to the fact that the result of the reaction is in high degree dependent on the amount of light which hits on every square centimeter surface of the reaction mixture; constance of light source, of distance of it from test tube and the time of lighting are, accordingly, absolutely indispensable in order to obtain reliable results comparable with one another. Schmidt has apparently had too little regard for these factors, for his results to be comparable with ours.

With this we have arrived at the conclusion and hope despite the criticism which we had to exercise on the Kottmann reaction — a criticism which does not refer to the clever basic idea of Kottmann concerning the realizability of which we have moreover no doubt, but refers to the present form of practical execution of his reaction and its significance — that we have shown that Kottmann has nevertheless through his method of serological thyroid examination shown a way which when once developed further, can bring valuable results to maturity.

Summary

1. The Kottmann reaction in the form described here for its practical execution, in so far as this may be judged from the cases investigated here, gives results in the sense that the sera developed according to it stain brown in varyingly marked degree; the most pronounced degree of browning is shown by the dwarf cretin sera; the weakest by the exophthalmic goiter sera; in between lie the sera of goitrous cretins, of ordinary goiters and the normal sera. The goiter venous blood sera show in general less marked degree of browning than the venous blood sera from the arm. The degree of brown coloration may be related more or less well (with several exceptions) with the clinical picture of the case in question.

2. If we disregard dwarf cretin sera and severe cases of exophthalmic goiter, the differences in degree of browning between the individual maximal developed sera are not very great.

3. These degrees of browning were measured on a Kollargol standard which remained constant for this.

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4. Concerning the relation between degree of dispersion and degree of browning there are not as yet any experimental investigations; Kottmann's opinion that the browner a serum developed by his method is, the more coarsely disperse its micelles, is accordingly not proved. The conditions seem to be quite complicated here.

5. Essential sources of error are connected with the Kottmann reaction, which are conditioned by the capriciousness of the silver iodide and of the colloid silver, with respect to their color and degree of dispersion.

6. The sequence of addition of the reagents, the type of light, are of great influence on the result of the reaction; a constant technique strictly adhered to in all experiments is accordingly an unconditional requirement in the execution of the reaction.

Practical Therapeutics

High Blood Pressure

THE intense interest displayed in recent years by profession and laity in high blood pressure is not of itself evidence that this condition is more frequent than formerly. The development of the clinical sphygmomanometer with the consequent ease in estimating blood pressure, the increased publicity given to life insurance and public health and mortality records, have all served to fix attention on this rather widespread condition of pathological physiology.

Hypertension is doubtless a precursor of arteriosclerosis and of general cardio-vascular disease but it is frequently, perhaps usually, found unassociated with these conditions. When associated with arteriosclerosis, however, the term "essential" hypertension is commonly applied.

The symptoms of arteriosclerosis, therefore, are chiefly the symptoms of the hypertension.

Toxic conditions have received much attention as a cause of hypertension and of arteriosclerosis, and it seems likely that a common toxic factor is the cause of both. Foci of infection, teeth, tonsils, chronic appendix, etc., metabolic diseases giving rise to toxic products of metabolism, have been related to both the arterial hypertension and the arterial changes. Obesity and diabetes likewise seem causative and suggest a toxic factor. Hartman and Ghrist (1), in a study of 2,09[illegible] cases taken from the records of the May Clinic, found, "The inconstancy of the diastolic readings emphasizes only the striking constancy of increase of systolic blood pressure with increasing weight in a non-selected group of office patients in a general practice."

In an exceedingly enlightening paper Blackford, Bowers and Baker (2) have shown the strong family tendency of this condition, its incidence after 50 years of age and its tendency to persist. They have analyzed the histories of 222 of 401 patients who were examined from 5 to 11 years ago. Their conclusions are:

"A study of 401 hypertensive patients (systolic pressure 175 or over) found in 10,000 clinical examinations made in a general clinic from five to eleven and one-half years ago has shown that:

"1. The appreciable incidence (1.2 per cent) of hypertension begins in the fourth decade; 5.8 per cent of all patients examined in the fifth decade showed hypertension, 12.3 per cent in the sixth, 22.5 per cent in the seventh, 14 per cent in the eighth, and 10 per cent in the ninth showed blood pressure above 175.

"2. Sixty-five per cent of the hyperten-

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sive cases in this series are in women; 50 per cent of all patients examined were women.

"3. The remarkably greater number of women having hypertension, as compared with men, comes in the fifth, sixth, and seventh decades.

"4. Family histories of hypertension were noted in more than one third of all histories.

"5. Cases of hypertensive disease complicated by goiter, syphilis, diabetes, chronic nephritis and valvular heart disease have each shown by groups no particular difference from cases of pure hypertension.

"A follow-up study of 222 of 401 hypertensive patients (55 per cent) examined from five to eleven and one-half years ago has been made. Twenty of these have been discarded for statistical study because they were moribund at the time of examination or died shortly afterward from other diseases. The 202 cases remaining, followed from five to eleven and one-half years, have shown:

"1. A gross mortality of 50 per cent, a male mortality of 70 per cent and a female mortality of 39 per cent.

"2. A mortality about the same for moderate and marked cases, but twice as high in extreme cases.

"3. An average duration of life after the first observation of thirty-two months for males and forty-four months for females.

"4. An average time since the first examination of 101 living patients of eighty-one months.

"5. Known causes of death, thirty-one from cerebral complications, twenty-five from heart disease, eighteen from uremia.

"We have not found any tendency toward recovery in hypertension.

"Occasionally remarkable exceptions are seen to the general rule of mortality. Women with hypertension sometimes outlive their expectancy. Men almost never do."

The treatment of hypertension falls under the general headings of hygiene, dietary and drug. O'Hare (3) says, "The care of such a patient should be based primarily on the knowledge that the problem is that of a generalized circulatory disorder consisting essentially of a functional vaso-constriction at first, then a more or less progressive small blood vessel sclerosis with superimposed vaso-constrictions, and finally as a result of cutting down of the blood supply to various organs, secondary degeneration and impaired function of these organs."

Rest, freedom from heavy muscular exertion, warm baths, mud baths, light treatment and the cultivation of habits of repose and efforts to relieve a tendency to worry are valuable. Excessive expenditure of nervous and physical energy should be guarded against. Diet, as a rule, is simply arranged by reducing the intake of food down to the energy requirement of the patient. In the overweight patient, reduction of diet and restriction of carbohydrates and fats are important.

For drug treatment, sodium and potassium iodide is classic. In cases with a history of syphilis they are valuable. Amyl nitrite by inhalation is valuable in controlling the sudden increases of pressure so frequently encountered. Nitro glycerin U.S.P. 1 minim by absorption from the mouth is to be used for the same purpose. Potassium sulphocyanate and bismuth subnitrate have recently received attention.

"Chemically pure potassium sulphocyanate was prescribed in a simple aqueous solution of such strength that 1 fluiddrachm (4 cc.) contains 1½ grains (0.1 gm.) of the salt. This dose was given in water by mouth three times daily, after meals, for the first week, twice daily for the second week and thence once daily for the third week of treatment. Thereafter this dose was given daily, or every other day." (4)

Bromides and luminal are most helpful in some cases characterized by nervous irritability. The effect of bismuth subnitrate on hypertension has been carefully studied by Stieglitz (5) who suggests the probable mech-

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The Doctor's Page



ARTHUR HARTMANN

(1849-).

The opportunity is not given to every one to serve his country in two wars and in a long interim between, to devote himself to successful private occupation so commendable as to obtain for him the highest honor of his state. In this respect Arthur Hartmann is unique.

He was born on January 1, 1849, in Heidelheim, a city situated near the eastern borde

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of Württemberg. His early life was uneventful. In Heidenheim and later in Stuttgart he received elementary and intermediate education, and at the age of 18 he sought entrance to the University of Tübingen for the purpose of studying medicine. After a little more than two years here his studies were interrupted by the war of 1870-1871, for he entered the military service as assistant physician in the Third Württemberg Field Hospital.

After the war Hartmann resumed studies at Freiburg and then at Leipzig, and in 1873 he was graduated from Leipzig. A brief activity as army physician occupied him until he undertook a journey to England, where he became acquainted with Lister, and to France. The years 1875 and 1876 Hartmann spent in Vienna studying especially diseases of the ear, nose and throat and after this extended period of preparation, in which he availed himself of much practical application he ventured definitely to set himself up as a doctor of diseases of the ear, nose and throat in Berlin (1876). The fact that he was found still practicing in Berlin 35 years later is meritorious. Excellent training in his subject and accurate diagnosis of the material presented soon won for Hartmann a reputation, not only in Germany but in other countries as well.

In order to satisfy an inclination to teach, Hartmann founded a polyclinic, where, from 1881 to 1894 he gave courses in his special subject. These lectures and classes were attended by physicians from all parts of the globe, who were desirous of acquiring the excellent technique of this man and of benefiting from the profound researches he carried on. In 1902 the title of Professor was bestowed upon him, in honor of his distinguished service. When the Rudolf Virchow Hospital was founded in 1905, Hartmann was called to the post of directing physician of the department of Diseases of the Ear, Nose and Throat. In 1909, his honorary titles culminated with that of *Geheimer Sanitätsrat*, the highest he could achieve. The following two years were crowded with much activity in his special field, and then he settled down for a well earned rest in his native city, Heidenheim. He turned his attention to social service, becoming the Director of the Society for the Improvement of Heidenheim; as an outgrowth of an interest in Uhland, he published a popular book referring to this locality and held a very successful exhibition of Uhland material in Tübingen. He was also identified with activities intending to curb the use and sale of alcoholic beverages in his province.

It was not long, however, before the tranquillity of his life was interrupted by the World War. He again entered the service of his country in medical capacity. In the early part of the conflict he was head physician in a hospital train, and later, though he had already led an active life passed his 65th year, he took charge of a reserve hospital until the end of the war.

Hartmann has contributed a great deal to the service of mankind, in his practice by the judicious application of knowledge gained from accurate pathological, anatomical and clinical investigations and by recording his findings in numerous scientific publications. Many of his writings, of which the greater part is composed of books or monographs, deal with diseases of the ear, nose and throat, and especially with deafness and dumbness and the education of the deaf and the dumb. Some of these are *Experimental Studies on the Function of the Eustachian Tubes* (1879), *Deaf-dumbness and the Education of the Deaf and Dumb* (1880), *Diseases of the Ear and Their Treatment* (1881) The success and reliability of the last two books have been so great as to more than justify their republication and translation from German into other languages. *Atlas on the Anatomy of the Frontal Sinus* (1900), *Textbook for the Instruction of the Deaf* (1909), *The Deaf Individual in the School* and *The Education of the Totally Deaf in Germany* (1912) render evidence that Hartmann not only treated his patients but also followed up with more permanent aid to those particularly afflicted with the handicaps of deafness and dumbness.

Hartmann broadened the scope of his literary activity when he took charge of the publication of *Zeitschrift für Ohrenheilkunde* after the death of Professor Moos. For a number of years the *Vierteljahresbericht* prospered under his expert supervision. From 1900 to 1904 he edited the *Verhandlungen der Deutschen Otologischen Gesellschaft* and became its President in 1906. Recently Hartmann has been attracted to the subject of nutrition and published, in 1928, a volume on *Nutrition and Raw Diet.*

During his active scientific career Professor Hartmann was interested in all things medical

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Medical Subjects by Famous Masters



"THE MONKEY DENTIST," by Michel Marie Charles Verlat (1824-1890)
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Editorial Comment

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Crystalline Ovarian Hormone

SINCE the preparation by Allen and Doisy of solutions containing the active estrus-producing hormone of the ovary, the activity of which was demonstrated by the vaginal smear method, there has been widespread activity in attempts to isolate the hormone as a pure crystalline substance. It is true that active extracts had been prepared before Allen and Doisy but they were of uncertain strength; the methods of preparation were complex and uncertain and there was no way of standardizing them or of comparing their values. The "lipoid" character of the ovarian hormone was first demonstrated by Iscovesco and his 11 Fb and V Dc, soluble in ether and alcohol, were among the best known preparations 15 years ago.

Seitz, Wintz and Fingerhut, Aschner, Frank, Rogers, Fellner, Herrmann and others made extracts of varying activity in the early period of study. The method of assay was more in the nature of a qualitative test — the effect on hypertrophy of uterus and tubes, on animal behavior, etc.

The introduction by Allen and Doisy of the Papanicolau-Stockard method of determining estrus by the vaginal smear method in 1923, made precise valuation possible and contributed enormously to all succeeding research.

The oily (lipoid) character of these preparations was a decided disadvantage and necessitated either the use of a bland inert oil for injection or the use of a colloidal aqueous solution.

Further research made clear, however, that although the active principle was extracted with lipoid solvents and was apparently itself a lipoid, it was possible to split the hormone from the oil and make a true water solution. Zondek, Laquer, Dickens and Dodd have been able to prepare these water-soluble preparations.

The estrus-producing hormone (as distinguished from the inhibiting hormone of the corpus luteum) may be obtained from the liquor folliculi of the ovary, from the placenta, from the blood, and from the urine of pregnant women.

Very recently Doisy, Veler and Thayer (1) have prepared the hormone in crystalline form.

"A crystalline product which has been recrystallized several times has been isolated from the urine. The assays show that the crystals are physiologically more active than any preparation obtained thus far, the activity being more than 2000 rat units per milligram."

This work of Doisy and his associates confirms the opinion of others that the principle obtained from liquor folliculi and the urine is the same. In the *Lancet* of January 4, 1930, it is reported that Dr. Butenandt of Göttingen has also produced a crystalline ovarian hormone.

"Butenandt worked with an oily material which was obtained from the urine of pregnant women, and contained about 30,000

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mouse-units per gramme. By repeated distribution between two solvents (aqueous alcohol and petroleum ether) inactive substances were removed in the petroleum ether fraction, and the material then had 500,000 mouse-units per gramme. This substance was further purified by the use of other solvents (ether, benzene, and ethyl acetate) and by adding alkali in increasing strength to the acid solution. An alkali-soluble fraction was obtained which had a mouse-unit of only 1.5 to 2 millionths of a gramme. Further purification was effected by distilling this oil in a vacuum of 0.20 — 0.03 mm. Hg and at a temperature of 130 — 150° C., and the material then contained 5,000,000 units per gramme. Sublimation in a high vacuum or treatment with solvents yields a crystalline product of which one gramme contains 8,000,000 mouse-units.

The development of a crystalline hormone of such astonishing potency is interesting in view of the lack of effects found by Frank at Mount Sinai Hospital, New York, in the case of practically all of the best known commercial products of a "purified" and "concentrated" estrous hormone.

The field of application in practical medicine of such a product is not yet demonstrated. Novak has pointed out the fundamental biological differences between estrus in lower animals and menstruation in the human female. Evolution has changed the process and altered the values of the several elements active in producing menstruation. In the human female the usual menstrual mechanism is greatly dependent upon the corpus luteum although the follicular hormone is, of course, important. Some cases may be observed in women in which there is a persistence of the more primitive follicular type of menstruation, but in general, human menstruation is not solely dependent upon the follicular hormone and it is not to be expected that this hormone alone will suffice in the treatment of irregularities of menstruation.

1. Doisy, E. A., Veler, C. D., and Thayer, S., *Am. J. Physiol., Abst.*, 1929, xc, 329.

Abstracts

The Ovarian Hormone and Its Site of Development. — W. Lahm. (*Zeitschr. ärztl. Fortbild.*, **26** : 78, 1929.)

The ovary accelerates ossification, controls sexual life, hair and growth of beard, development of baldness, pigment metabolism, tonus of the blood vessels, metabolism in the capsular ligaments (arthritis ovaripriva). Primary agenitalism is combined with hypotonia. In the climacteric the ovarian deficiency causes hypertonia. The generative function might also be the object of certain internal secretory relations. The most recent experimental investigations favor the idea that the disintegration of the ova and their resorption excite vegetative impulse. The substances which induce the growth impulse in the uterus — ovarian hormone — were originally obtained from the ovary. Today we know that numerous albumin substances, histamin, etc., can exert a growth stimulus on the uterus. The following requirements were set for the ovarian hormone: lipoid solubility, indestructibility (indestructibility even through digestion), specific activity, preparation from ovary, placenta, blood or urine.

Hypoglycemic Action of Combined Borate and Insulin. — Loeper, Ravier and Tonnet. (*Progrès méd.*, **47** : 189, 1929.)

The authors undertook experiments on four diabetic patients. Their blood sugar varied from 2 gm. to 3.50 gm. The patients first received injections of pure insulin; to the second injection, 0.45 or 0.90 sodium borate was added. In two cases the strengthening of the insulin effect and the reduction of sugar excretion through the combination with sodium borate were evident. In one case the inverse effect occurred: the combined injection had less of an effect than pure insulin injection.

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Concerning the Hormonal Therapy of Ovarian Hemorrhages. — Kraul. (*Wien. klin. Wochenschr.*, 42 : 158, 1929.)

Demonstration of a series of youthful patients in whom transfusions of 100 to 150 cc. of blood of pregnant women were undertaken on account of profuse, irregular hemorrhages, after styptics, curettements and irradiation of the spleen had remained without effect. Kraul considers the action of injections of blood of pregnant women to be the result of the hormone content of the pregnant blood, in favor of which the lasting success of the treatment also speaks.

Hypogenitalism. — Serdukoff. (*Progrès méd.*, 21 : 901, May 25, 1929.)

By hypogenitalism is meant the various endocrine disorders intimately connected with decrease, disappearance or absence of the genital glands. In women, the period of puberty and that of the menopause may be regarded as the manifestations of a physiological hypogenitalism; just as there are endocrinopathies with distinctly pathological tendency such as chlorosis and eunuchoidism.

Chlorosis is one of the affections observed exclusively in girls at the time of pubertal development. This condition is intimately connected with the decrease in internal secretion of the ovaries or with the delay in formation of the endocrine products of these glands. The greater number of symptoms of chlorosis indicates hyposecretion; certain ones may be explained as being the result of an autointoxication due to dysfunction of the endocrine glands. Chlorosis is regarded as a pluriglandular affection: in addition to the ovaries, the thyroid and pituitary are also involved.

In the amenorrheic forms of chlorosis good results of treatment are obtained by different organotherapeutic preparations extracted from ovarian substance, especially in combination with iron. In the menorrhagic forms it is logical to prescribe preparations of pituitary. In general medical treatment should be associated with regulation of living conditions and principles of general hygiene to aid the organism in the critical time of puberty.

Individuals are designated as eunuchoids who give the impression of castrates, even though their genital glands have not been extirpated. The genital insufficiency to which the various forms of eunuchoidism are related may present a symptom complex identical to that arising after complete ablation of the genital glands. Congenital or natural eunuchoidism is the result of congenital aplasia of the sexual glands; there are also atypical forms of eunuchoidism. From the clinical viewpoint in women totally castrated a characteristic symptom complex develops: menstruation is arrested. Later there appears atrophy of the mammary glands, of the external genital organs and of the uterus. There is retardation of development of the bones of the pelvis and of the lower extremities in the castrated woman. General appearance changes and the patients acquire masculine traits. Then, as result of the lack of endocrine influence of the ovaries, vasomotor, secretory, emotional and psychic disorders develop. There is also observed disturbance of general metabolism. The post-operative disorders are not so manifest after castration of mature women. Congenital eunuchoidism is rare. The symptoms of eunuchoidism correspond to those observed in castrated women: osseous modifications as well as absence or total disappearance of hair; menstruation is missing in typical cases; sexual desire is wanting.

Eunuchoidism is intimately related to deficiency of function of the genital glands. Among the number of etiological causes there is admitted emotional shock during intrauterine life. Traumatisms, infections and septic affections with destruction of the parenchyma of the genital glands may be related among the principal etiological causes of the late secondary forms of eunuchoid degeneration.

The differential diagnosis of eunuchoidism does not present any great difficulties in typical cases with definite symptom complex. The results of treatment are variable according to whether ovarian tissue capable of functioning is present or not. Most frequently treatment is symptomatic. Organotherapy may be applied by mouth or in injections; various ovarian preparations being used. In general, injections are most recommended. In certain cases of hypogenitalism and in particular in certain forms of hypoövarianism and eunuchoidism, there is noted decrease in sexual desire. In these cases associated treatment (ovarian preparations and yohimbin) is recommended. In cases where the symptoms of hypogenitalism are especially marked in the osseous system, it is good to apply combined treatment with ovary and calcium. In cases where primary lesions

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of the genital glands are associated with pluriglandular disturbances, treatment with thyroid or pituitary must be associated with ovarian treatment.

When eunuchoidism in women is accompanied by obesity, loss of hair and modifications of metabolism with retardation of the process of oxidation good results may be obtained with treatment by minimum or moderate doses of thyroid. In certain cases the symptoms of obesity psychic apathy, intellectual indifference, weakness of memory, muscular fatigue, fall of hair yield to associated treatment with the three principal glands of the organism: ovary, pituitary and thyroid.

In cases of total absence of the genital glands, after castration or in congenital eunuchoidism, the modifications assume so tenacious a character that treatment with simple or complex endocrine preparations remains unsuccessful.

The most real method of treatment at the present time applied to cases of eunuchoidism hypoövarianism and other forms of the hypogenital syndrome is the transplantation of endocrine glands. The transplantation of genital glands in eunuchoidism (homo- or hetero-transplantation) produces a good stimulatory effect. The transplantation often contributes to the arrest of atrophic processes of genital involution in the case of secondary eunuchoidism. In the primary forms of genital eunuchoidism transplantation of the ovaries relieves the painful nervous, vasomotor, psychic and somatic symptoms.

Hyperthyroidism Evolving towards Hypothyroidism in the Course of a Treatment with Iodin. — L. Dautrebande. (*Presse méd.*, **37** : 721, June 1, 1929.)

The author reports a case of a young man of 20 years with goiter and hyperthyroidism which was transformed into hypothyroidism during an iodin treatment. He calls attention to three interesting points in this clinical observation: (1) a definite case of hyperthyroidism may be transformed into hypothyroidism under the influence of iodin. The author observed another case where the metabolism fell from +10 to −11 after 3 weeks of treatment and rose again immediately afterward. With Lemort, he also observed a third case where the hypothyroidism attained −20 per cent but was transient. This is the first time, the author believes, that the appearance of a prolonged hypothyroidism following administration of iodin has been reported. (2) The second interesting point is a change in the exterior appearance and intellectual habitus of the patient during the treatment. This change is paradoxical as the patient observed distinct signs of cretinism disappear at the time when his metabolism had been below normal for several weeks. (3) Finally a third point of this case report is worthy of mention: the coincidence of a definite hyperthyroidism with a soft goiter without nodules appearing clinically as a simple colloid goiter of adolescence and the transformation of this simple hyperthyroid goiter into a hard adenomatous protuberant goiter contemporaneous with a hypothyroidism, whereas this type of hard goiter is frequently the accompaniment of toxic hyperthyroidism.

Clinical examination alone is not sufficient for drawing a conclusion of hyperfunction or hypofunction of a thyroid; determination of the basal metabolism remains the indispensable diagnostic aid.

Further Investigations in the Preparation, Biology and Clinic of Pituitary Anterior Lobe Hormone. — B. Zondek. (*Klin. Wochenschr.*, **8** : 157, 1929.)

The anterior lobe hormone is a very sensitive substance which in contrast to folliculin is destroyed by cooking, acids and alkalis. Whereas folliculin is soluble in ether anterior lobe hormone is insoluble in the majority of lipoid solvents, so that (for example in the preparation from urine of pregnant women) a separation of the two hormones is possible thereby. In the preparation of the hormone from the pituitary anterior lobe, placenta and pregnant urine, results are least objectionable and the gain is better by the way of precipitation which the author uses for the past 1½ years. It could be determined that pituitary anterior lobe hormone is precipitated under certain conditions through a series of organic solvents miscible with water (for example, ether, alcohol, methyl alcohol, acetone, etc.).

With dissolution of the precipitant in water there remains an insoluble residue which does not contain the hormone, so that in this way also a further purification is possible. The desiccated substance remaining, containing the hormone, is soluble in water.

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The author's investigations were undertaken on sexually mature (1600 to 1800 gm. weight) animals, as well as infantile animals (1100 gm.). Following 10 to 14 days of treatment (2 to 4 cc. pituitary anterior lobe extract equals 60 to 120 rat units *pro die*) there was shown a powerful influence of pituitary anterior lobe extract on the genital apparatus. The uteri had been transformed from thread-like tubes to formations as thick as one's finger (blue-red, livid in color) which contract immediately upon the stimulation of opening of the abdomen. In infantile animals one had the impression of a young pregnancy. The ovaries, of the size of lentils, became almost as large as cherries, replete with blood dots and golden yellow corpora lutea. Sections through the vagina showed less changes of the mucosa, especially increase in thickness of the vaginal musculature. The uterus showed this growth under the action of pituitary anterior lobe in still more pronounced degree. Here especially the markedly polypous proliferated uterine mucosa is conspicuous which is quite similar to a pregnancy mucosa in the rabbit. In the ovary the primordial follicles are displaced on the border zones in consequence of blood-filled luteinized follicle, in which in addition to the granular proliferation, the splendidly developed theca must especially be referred to. In the discussion, Aschheim could demonstrate the isolated, partly luteinized theca proliferation in the mouse under the action of pituitary anterior lobe.

The author knows little concerning the clinical action of pituitary anterior lobe extract in human beings, since he has used it only for the past ¾ year in the clinic.

Clinically the author was able to determine that anterior pituitary intramuscularly injected has a marked hyperemic influence on the female genital apparatus so that a picture of a young pregnancy can be simulated by turgor and color. This action determined through direct contemplation in operations he found corroborated thermometrically. The author was able to determine a rise in temperature of the peritoneum, which lay not as usual at 0.5°, but up to 1° above the axillary temperature. This pelvic hyperemia can doubtless be utilized clinically. Following a suggestion of P. Klein anterior pituitary extract is being used by the author in the University Clinic for Women of Charité, Berlin, in inflammatory pelvic affections in women, in order to induce the therapeutic effect through the hyperemia.

Through pituitary anterior lobe extract a stimulus to ovarian function in women is exerted and through it secondarily on the structure of the uterine mucosa. If one injects pituitary anterior lobe extract from the first day of menstruation to the eighth day of the cycle and then examines the uterine mucosa, a structural stage is found in this, which corresponds to about the 14th to 16th day of the cycle, the beginning of the secretion phase.

Concerning the Influence of Thyroxin on the Metabolism of Surviving Tissue. — K. J. Anselmino, O. Eichler and H. Schlossmann. (*Biochem. Zeitschr.*, **205** : 481, 1929.)

The reports in the literature concerning the action of thyroid hormone on respiration and fermentation of surviving cells are contradictory. The results of experiments which the authors carried out showed as the most striking change the increase of anaerobic glycolysis of the kidneys.

In sections of spleen, liver and kidneys of white rats 24 hours to 7 days following injection of thyroxin only a very slight or no increase in respiration was found, measured by means of Warburg's method. The anaerobic glycolysis of the kidney increases all the higher the stronger the increase of consumption of oxygen effect in the living animal through the thyroxin. The anaerobic glycolysis of the liver and spleen is not increased. The experiments prove that the thyroid hormone attacks the anaerobic phase of the metabolism in the first place.

On the Female Sex Hormone. III. Contribution. The Activity of the Estrous Hormone by Oral Administration. — F. Lange and W. Faure. (*Deut. med. Wochenschr.*, **52** : 310, 1926.)

With the value determination procedures given by the authors, it can be shown for the mouse by clear estrous cycle curves that the ovarian hormone is also effective by oral administration. Approximately a twenty times greater amount is needed, however, *per os*, than is effective subcutaneously. Important conclusions may be drawn from this experience for therapy. The active value of the best ovarian preparation for oral administration tested, was never over one mouse unit per single dose. If a mouse unit

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is placed as a basis for the assigned requirement *per dosis*, the authors calculate that 500 dragees *per diem* would be required for a preparation. However, the question whether a mouse unit will be sufficient to attain an effective amount of hormone in the organism, is more than questionable on the basis of experiments on rats (five times heavier in comparison with mice). From determinations on the blood of women, it could be calculated that 50 to 150 mouse units circulate in the total amount of blood. If we estimate at 1 to 2 days the duration of the effect with the unusually stable ovarian hormone, that amount must be given in this period (through substitution therapy in deficiency of ovarian function) which takes into consideration the fact that only 1/20 of the hormone value comes to active development by oral administration.

The Content of the Human Pituitary in Melanophore Hormone. — K. Ehrhardt. (*Münch. med. Wochenschr.*, **76** : 321, 1929.)

The author examined 50 pituitaries of human corpses in order to test whether that agent which brings the frog melanophores to expansion (melanophore hormones) is regularly contained therein. The results of investigation are: (1) The melanophore hormone is almost regularly contained in the human pituitary (in 48 of 50 cases examined). (2) The melanophore hormone is also visible in the pituitary of old people and of the newborn. (3) The melanophore hormone was missing in the pituitary of a patient who died of paralysis and in a patient whose autopsy showed typical Laennec liver cirrhosis.

In conclusion, the author states: there exist in adolescence and even in childhood pituitary adenomas amenable to radiotherapy. When they are accompanied by osseous lesions which characterize gigantism or acromegaly, their diagnosis is easy. In the absence of osseous lesions and especially with symptoms of infantilism, the differential diagnosis between these adenomas and tumors of Rathke's pouch offers great difficulties. In doubtful cases when radiography of the skull does not reveal supra- or intra-sellar calcifications considered to be pathognomonic of tumors of Rathke's pouch, the possibility of adenoma must be thought of and radiotherapy be resorted to, at least as trial, to replace it by surgical treatment as soon as aggravation of symptoms principally of visual disorders, shows the ineffectiveness of this test.

Organotherapy in Cancer. — Rous-Sergent. (*J. praticiens*, **43** : 319, 1929.)

According to the few observations reported by Naamé the idea should not awaken in physicians that organotherapy in cancer can play a rôle as active treatment. The observations reported merely show that the general condition of the patient was improved. It would be inadmissible to speak of a cure. Moreover, Sergent was never able to observe improvement in the anti-cancer center of Villejuif; he does not mention recoveries observed such as those reported by Naamé.

Pituitary Adenoma of Adolescence and of Childhood Amenable to Radiotherapy. — A. Béclère. (*Rev. neurol.*, **1** : 463, No. 3, Mar., 1929.)

Gigantism and acromegaly either associated or isolated are the clinical manifestations of chromophil adenomas. Gigantism always begins before the age of 20 years, either at the beginning of adolescence or often from childhood, sometimes before the period of puberty and sometimes after it. Such was the case of a young girl of 16½ years in whom the author obtained the first lasting success with radiotherapy. This was 20 years ago and results have been permanent.

The form which is principally ophthalmic with or without symptoms of hypopituitarism, is the clinical manifestation of chromophobe adenoma. Dott and Bailey report in detail the observation of a chromophobe adenoma of adolescence with partial infantilism erroneously diagnosed as a cyst of Rathke's pouch, operated by transfrontal route with considerable improvement of the vision and irradiated later.

In some cases of gigantism the syndrome of infantilism is more marked and more complete simulates the clinical picture of tumors of Rathke's pouch. Finally among the observations of pituitary tumors more or less improved by radiotherapy, which Dr. Sol... mon reported to the International Neurological Congress in 1928, three concerned children from 11 to 12 years.

Precocious Glandular Obesity with Optic Atrophy. — F. Terrien, H. Schaeffer and J. Blum. (*Rev. neurol.*, **1** : 798, No. 5, May, 1929.)

The patient, a child of 5 years, weighing 32 kg., presented bilateral optic atrophy with

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white papillae and excessive obesity, involving the trunk and members, but predominating at the pelvis, buttocks, pubis and lower members, whereas the face, neck, feet and hands seem almost immune, as in the adiposogenital syndrome. This child presents a bilateral cryptorchidism; the sella turcica is abnormally enlarged; the thyroid seems small. There is no neurosomatic sign; intelligence is normal. Wassermann reaction is negative in the blood. The obesity and blindness seem to have developed parallel from the first months of life. In this case the author questions whether the optic atrophy is dependent upon the chiasmatic compression by a pituitary neoplasm or if the blindness and obesity do not arise from the same heredosyphilitic cause.

Studies on the Influence of Substitution in the Thyroxin Molecule on the Action of Thyroxin. — Abderhalden and Werthheimer. (*Zeitschr. exp. Med.*, **63** : 4-5, 1929.)

Closely related combinations of thyroxin were tested for their action with respect to the development and growth of tadpoles and axolotls as well as for gas metabolism in rats. On the whole fourteen combinations were tested. In the first place the problem is to determine definitely whether the specific action of the thyroxin bound to the iodid atom in the molecule, either wholly or in part by Cl or Br, could be substituted. The de-iodized thyroxin proves inactive in substitute combinations, a fact of particular significance, in general it proves active when in higher concentration. This holds good even for di-iodid thyroxin, that is after cleavage of one iodized oxy-phenyl group of the thyroxin. There is naturally, the possibility that the substitution product of thyroxin in the organism will be changed back; it is also possible that the action of thyroxin itself is not strongly specific.

Concerning the Biology of Placenta Extract. — Gräfenberg. (*Klin. Wochenschr.*, viii, 1376, 1929.)

Injections of placenta extract into animals have a negative Allen-Doisy reaction. In human beings in which an injection is justified following hemorrhage in pregnancy, they have a diagnostic value. Placenta extract works favorably in the interruption of internal secretions.

Of Course the Patient Came Back

The young woman with dysmenorrhea who receives palliatives will return, because the disturbance of menstruation is still present. But sooner or later she "tries" another physician. Endocrine therapy which gradually relieves the pain by correcting the faulty menstrual process makes a favorable impression on the patient and her family.

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Atrophy of the Genitals and the Hormone of the Anterior Lobe of the Pituitary. — K. Erhardt. (*Münch. med. Wochenschr.*, **76**, No. 30, 1929.)

During a ten months observation of the blood and urine of a 35 year old patient with intense atrophy of the genitals and chronic paranoid mental disturbance, there was found a permanent positive reaction to the anterior lobe of the pituitary. In contrast to this very rare case, the next almost inexplicable observation is a relatively frequent transient positive reaction to the anterior lobe. This was found, though in no way regularly, in women castrated by means of the X-ray and in totally extirpated women, in cases of genital carcinoma, uterus myomatosus, epithelioma of the chorion, acromegaly and pituitary tumor, at the beginning of the menopause and in climacterium praecox, in amenorrhea, lipoid kidney and after the transfusion of 500 cc. of blood from a pregnant woman. On the basis of over 300 cases (experimental results of 2000 tests) the reliability of the Zondek-Aschheim pregnancy reaction has been confirmed.

Attack of Hypersomnia in a Patient with Thomsen's Disease: Remarkable Action of Insulin. — J. A. Barre. (*Presse méd.*, **37** : 1029, 1929.)

In an individual afflicted with Thomsen's disease there occurred at times, or daily, attacks of uncontrollable lethargy, deep and of long duration, out of which he could be aroused only with great effort.

Daily injections of 7-10 units of endo-pancreatic extract (insulin) caused this condition to disappear rapidly. Sleeplessness replaced the lethargy and the treatment had to be stopped.

Concerning the Endocrinology of and Therapy of Pathological Menstrual Hemorrhages in the Age of Development. — E. Glaesmer. (*Münch. med. Wochenschr.*, **76** : 406, 1929.)

It is a question of therapeutic experiment and result in a great series of menstrual anomalies in girls between 16 and 22 years who in the majority of cases exhibit "irritable hemorrhages" and in the preponderant number of cases a more or less marked genital hypoplasia.

A treatment of these irritable hemorrhages must *a priori* strive against an influencing of the follicular apparatus. The author attempted to exert this influence through cholin. Injections of cholin gave the same action in animal experiment as radioactive irradiation. Cholin is a constant constituent of many tissues. Owing to its blood-pressure lowering effect a hormonal property opposite to the adrenalin action is ascribed to it. The therapeutic experiences of the author are limited only to the field of the increased hemorrhages accompanying hypogenitalism at the age of development, and are favorable throughout. The results of the treatment were almost entirely good. In just as startling a manner, however, cholin acted on puerile hemorrhages resting on infantile basis. The most suitable preparation for cholin treatment proved to be borate of cholin. Cholin is superior to weak irradiation, since it requires neither expensive apparatus nor difficult technique and renders possible much more accurate dosage.

The Internal Secretions and the Problem of Rejuvenation (Experimental and Clinical Trial). — N. E. Ischlondski. (*Progrès méd.*, **44** : 767, May 4, 1929.)

The scientific study of the problem of rejuvenation is founded on the following biological conception: the genital glands secrete a specific hormone into the blood which circulating in the organism assures the development, then the preservation of the specific sexual constitution, one of the most characteristic pictures of youth. The most intimate relations exist between the genital glands and all the rest of the endocrine apparatus; the decrease or increase of internal secretion of the genital gland reflects on the activity of the other endocrine glands such as the pituitary, thyroid, etc. The aim of rejuvenation is reduced to stimulating the activity of the whole complex of the endocrine glands by the inoculation of an internal secretion, most frequently the sexual secretion. Without this intermediary stage, without the endocrine apparatus as a whole, there can be no question of a general rejuvenation. There are three stages to be distinguished in the story of the practical realization of the problem of rejuvenation. In the beginning we were limited to the transplantation of genital gland from a young animal to an old. The success of the operation in small mammals is unquestionable. In man this operation can not be executed for two reasons. (1) A practical impediment — the absence of human materi-

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for the transplantation. (2). A scientific consideration: the fate of each transplant depends on the regenerative capacity of the animal organism. This latter power is definitely manifested by lower animals and diminishes progressively in the more differentiated organisms.

In the face of the impossibility of transplantation of the sexual gland in man, the investigators have sought other means of action on the apparatus with internal secretion. Steinach himself tried to replace homoplastic transplantation of the gland by ligature of the canal deferens of the gland of the aged organism. Voronoff decided to use heteroplastic material (glands of anthropoid apes).

The author considers the results obtained by heteroplastic transplantation to be due to non-specific protein therapy. He arrives at the conclusion that the surgical method of rejuvenation viewed from the practical viewpoint at least at the present time, loses its importance. In his personal works on the application of the internal secretion of the genital glands the author made efforts to elaborate a chemico-biological method having as goal the extraction of the pure sexual hormone to be injected into the blood by parenteral route. A series of systematic works in the indicated direction has shown that a great quantity of the stimulating substances is found in the region of the hepatic tissue, embryonic tissue and placenta. Towards the end of the year 1924, the author was able to extract the genital incretion in its active form. Before undertaking the study of the action of the isolated internal secretion he had to elaborate an objective criterion to determine its action scientifically. The product given contains the active genital secretion only in the case where the introduction of this product into the organism realizes all the modifications in secondary sexual characters which Steinach was able to obtain by surgery. If this condition is not accomplished, the product can not claim the name endocrine.

The results of investigations on the rejuvenation of old, enfeebled animals were very encouraging. The experiences of the author prove not only that an effect of regeneration of the animal organism may be produced but also that the result obtained represents an actual rejuvenation, since it signifies a very distinct prolongation of life.

The author then began to systematically study the effect of the extract on man. Cases of senility in subjects from 60 to 82 years of age (32 cases); cases of psychic old age (4 cases); cases of precocious senility at the age of 34 to 50 years (31 cases); definite cases of weakness or complete arrest of sexual function in men aged 32 to 55 years (22 cases); cases of sexual insufficiency and hypo-development related to general asthenia in young girls (12 cases); cases of decrease of general metabolism and asthenia with varying etiology (11 cases); severe forms of anemia in the two sexes (18 cases). After treatment with the extract the patients showed an increase in strength and physical resistance.

One of the early signs of the action of the secretion was the restitution of normal sleep. In all patients a considerable increase of appetite was soon noted. There was increase of weight. A beneficial effect on constipation was also noted. In all cases where objective disorders of the blood were observed, these disturbances disappeared. There was a considerable increase in the number of red blood corpuscles. The action produced on sexual function enfeebled by age or prematurely was very remarkable. Even in cases of prolonged and resistant impotence treated unsuccessfully by various methods the author succeeded in raising considerably or restoring *in toto* the lost function. It is very important as characteristic of this action that after a treatment of short duration (12 injections) the action continues to increase and develop during long months after the treatment to become stabilized definitively. Relative to the restitution of the weakened or absent sexual function in women, most frequently in asthenic and underdeveloped young girls, 1 to 3 injections of feminine internal secretion suffice to cause a reappearance of menstruation. The author also mentions the beneficial action of the secretion in cases of disorders of the menopause: in cases of amenorrhea and dysmenorrhea. Quite an exceptional rôle may also be given to the action of the secretion on the psyche. An important rôle belonging to the second category of influences of the secretion on neuropsychic activity of the organism is also described: the action on memory, attention and capacity for concentration, the influence on the skin also presents considerable interest from the scientific as well as the practical viewpoint; it becomes more elastic as turgescence increases. During the experiments on ani-

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mals a considerable increase in resistance of the organism to infections due to the action of the secretion was noted. This was also observed in man.

The secretion does not act directly on the separate functions but regenerates the mechanisms of the organism itself: in the first place the internal secretory apparatus and the central nervous system. From the theoretical viewpoint this signifies that the fundamental principle of the influence does not present a substitution of substances lacking in the blood but rather a specific therapy of stimulation of activity of the endocrine glands.

The Action of Parathyroid Hormone on Tetania Parathyreopriva. — A. W. Elmer and M. Scheps. (*Klin. Wochenschr.*, 8 : 1407, 1929.)

On the basis of extensive researches the authors came to the following conclusions. Parathyroid hormone has a specific action on Tetania parathyreopriva.

The action of the parathyroid hormone surpasses by far that of other mediums. Treatment with parathyroid hormone by subcutaneous injection acts, within 5 to 15 hours in such a way as to quickly ameliorate the clinical evidences of tetany. In the worst tetany cases, where immediate aid is necessary intravenous injection of parathyroid simultaneous with the subcutaneous injection is required, which will bring apoplectiform recovery within 20 minutes to 1½ hours. The intestinal treatment with parathyroid hormone is also indicated in most of the more severe cases of tetany, especially in those in which other measures have failed.

Parallel with effecting amelioration of the clinical picture the parathyroid hormone influences the blood chemistry in that above all it intensifies the blood picture; it decreases the phosphorus and potassium. The influence of the alkali reserve and of the coagulation time is not constant.

The dosage of parathyroid hormone must be calculated individually and under the control of calcium content of the blood.

The duration of treatment with parathyroid hormone is varied. In acute cases with only transitory insufficiency it should only be administered during the existence of the clinical symptom; in most of the severe chronic cases it should be administered, similar to treatment with insulin, continually or with short pauses, and at best with simultaneous administration, *per os*, of calcium.

Evidences of a hypercalcemic syndrome were not constant.

The Properties of General Regeneration Hormones. — Fränkel. (*Arch. klin. Chir.*, clv, No. 2, 1929.)

In a first piece of work the author showed that the healing process after fracture of the femur presents a varied aspect in cases of bilateral fracture and particularly different when the fractures are not simultaneous. In a second essay Fraenkel showed that this variation reverts to two different hormones, to the plastic hormone and to the hormone of regeneration; their concentration in the blood varies even considering the state of tissue in regeneration. In this new work the author attempts to determine the action of the hormone. In his opinion the plastic hormone acts first for the development of new tissue and then prepares the tissue, through sensitization, for the action of the hormone of differentiation. Lastly it might have a threefold function: it stops the development of new tissue, at the same time it activates the differentiation and the destruction of these tissues. Its action on young regeneration tissue is insignificant, as on old tissue.

Observations on the Changes of Permeability by Means of Thyroxin. — A. Fröhlich and E. Zak.

The researches of these authors portend that permeability in March (tested in frogs bred in winter) is significantly poorer than in autumn (tested in frogs bred in summer). Treatment with theophyllin improves the poor permeability of winter frogs and in contrast decreases the better permeability of summer frogs for potassium iodide.

Further researches showed, for the case of potassium iodide, that, to a certain extent, the nervous system co-operates in the influence of theophyllin on the tissue, while the action of this diuretic in the case of grape sugar is without the participation of the nervous system. Now follows the researches of Cori, namely that the hyperexcitability of the sympathetic nerve in summer, which is indeed capable of overshadowing the effect of the simultaneously stimulated vagus, is dependent upon the thyroid gland which is active during the summer. It seemed of interest, therefore, to inquire whether, by the

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dministration of thyroxin to winter frogs that had previously been treated with theophyllin, a modification would be induced that would be similar to that in summer frogs treated with theophyllin alone.

For this purpose edible winter frogs were preparatorily treated in March, 1929, with thyroxin. The animals remained under this process for about three weeks, they were treated in practically the same manner as those of March, 1927 and 1928, with exactly the same experimental procedure; four injections of 0.3 cc. Henning's thyroxin solution were given subcutaneously. These animals were then daily, in the usual manner, perfused with theophyllin and potassium iodide Ringer solution containing 0.1 per cent potassium iodide).

The result of this experiment was that winter frogs previously treated with thyroxin plus theophyllin responded, in degree of permeability to potassium iodide, approximately the same as summer frogs treated with theophyllin alone; therefore it was possible the year round, to simulate the influence of the summer months in this respect.

Rectal Liver Therapy. — A. Hittmair. (*Deut. med. Wochenschr.*, lv, 398, 1929.)

In two cases of pernicious anemia that refused the oral administration of liver, a test was made by giving liver broth as an enema. In one case the test failed, the other case became profusely diarrhetic. In additional instances 300 gm. of liver from liver preparations, in suitable quantity was given daily in the form of suppositories. In some diarrhea again ensued, in some the test was satisfactory, but not so satisfactory as when liver was administered by mouth. In time the administration of small enemas with the addition of liver preparations will be tested.

Concerning the Relation between the Endocrine Glands and Abortion. — E. Imparato. (*Monde méd.*, xxxix, 793, 1929.)

It is not yet understood what is concerned in the recovery from abortion. The author offers a series of opinions of various authors and on the basis of his own observations he comes to the following conclusion.

From the literature and from his own experiments it can be concluded that abortion is allied with the insufficient activity of glands and that in the pathogenesis of this disease the ovary plays a significant part. It is true that in the treatment of the above mentioned disease with organotherapeutic products there have been both good results and failures, but with the limited knowledge we possess of the physiology and pathology of the internal gland secretions, one must be very cautious when he directs his attention to abortion or refutes it.

The Increase of Erythrocytes following a Secretin Injection Is Principally Traced Back to the Spleen. — F. W. Krzywanek. (*Pflügers Arch. ges. Physiol.*, ccxxii, 435, 1929.)

The influence of secretin solution from the dried small intestine (duodenum) of dogs was tested on normal dogs. In each case, at various intervals after the injection, a considerable definite increase in percentage of blood cells occurred, that varied between 22.5 and 34.5%. This finding coincides with the results of other authors; the explanation that this increase was a new formation or a thickening of the blood was refused for the reason that the factor in this case was the function of the spleen; for in animals with the spleen removed such a rise after secretin injection was not at all evident, or at least in only a very few cases.

Concerning the Biology of Placenta Extracts. — Gräfenberg. (*Zentr. Gynäkol.*, liii, 1795, 1929.)

Placenta extract derived according to the method of Coca showed in experiments with mice, a negative Allen-Doisy and a negative Zondek-Aschheim reaction. It was evident that the testicles of male animals treated with this extract were smaller than the testicles of untreated control animals. The extract effected no abortive action and did not respond in anaphylactic tests on guinea pigs, furthermore, no complement-building substance was derived in rabbits. In spite of these negative results in experimental animals the extracts were valid diagnostically in human beings. The albuminous extracts are a fine reagent. Skin tests on pregnant women often give a specific wheal picture, but a conjunctival reaction is not evident. One injection of the extract following hemorrhage intercepts pregnancy; however, an abortive action fails. The results with placenta extracts are favorable for the interruption of

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internal secretions. In its biological properties placenta extract shows noteworthy relations to allergic extract.

Folliculin in Amenorrhea. — Laffont and Chiapponi. (*Bull. Soc. Obstet. et Gynecol. Paris*, No. 6, 426, 1929.)

In a case of dysmenorrhea and amenorrhea a total recovery was obtained by treatment with folliculin. The doses administered were 60 units in 3 days. In another instance in which larger doses were given, the results obtained were not in accord with the others. Both instances demonstrate again that the influence of folliculin on menstruation is not yet comprehensible. Certainly the folliculin possesses an undoubted activity, but the ways and means of administration requires the proof of researches. Clinical observations and the results of research on the estrus in the laboratory must supplement each other.

The Value of Contractility of the Spleen Induced by Adrenalin in the Practical Clinic. — Jean Lerebouillet. (*Paris méd.*, xix, 79, 1929.)

V. Simone (*Minerva med.*, May, 1929) studied the applicability for clinical medicine of contractility of the spleen induced by the administration of adrenalin. Adrenalin gives satisfactory results in the diagnosis of latent malaria particularly in those forms in which the histological changes of the spleen have not yet brought about the contractility. In the treatment of malaria and the suprarenal insufficiency induced by it, it is profitable to combine adrenalin with quinine.

The adrenalin experiments can be adapted with caution in the diagnosis of cryptogenic septicemia, but only if the ejection of the microorganisms of the disease, stagnating in the spleen, do not threaten to become worse. In fact adrenalin can provoke the relapse to typhus and Malta fever or endocarditis lenta. Furthermore, one must always keep in mind the possibility of rupture of the spleen itself or of cysts or abscesses of the spleen, and hemorrhages which result from a violent expulsion of blood through the extension or constriction of the collateral veins, and instances of thrombosis of the splenic veins are also to be feared, therefore, adrenalin can only be used after great deliberation.

In therapy adrenalin can be applied to many cases of splenomegaly in which one has to consider a spleen tonus following the di turbance of the circulation; thereby a sort functional splenectomy can be attained certain diseases in which the hemorrhag infarct of the spleen plays an important par as is the case in many forms of hemolyt icterus. Lastly, by preliminary adrenal injections by means of which the blood hel in the spleen will be evacuated precautio will be had against the loss of a great quantit of blood in splenectomy.

Liver Therapy of Anemia in Nurslings and Young Children. — Jerachmiel Ligum (*Monatsschr. Kinderheilk.*, xliii, 513, 1929.)

The author treated twelve cases of anemia of various sources in children with liver diet. In prematurely born children this therap induced an increase of hemoglobin from 62 t 74% and an increase of erythrocytes fro 2,930,000 to 4,400,000 resulted. It is possibl to administer large doses of liver to olde nurslings much more readily than to the pre maturely born. In one instance, with pre maturely born treated with raw liver juice treatment had to be abandoned because thi stools resulted. Children in the first yea accept liver readily, however, in children tha have a distaste for it, liver therapy does no act favorably. In one case dyspepsia followe treatment and no result could be obtained In most children from 1-6 years good result were obtained with liver therapy and a increase of hemoglobin as well as erythrocyte resulted.

The action of the liver must evidently b founded in part on the iron content of th liver; more likely the profusion of vitamine in liver gives the significant results in trea ment. Liver contains all vitamines, especiall Vitamine A, B and C, in large quantities Herz in Hamburg agrees that good result were obtained in the treatment of anemia o children with the liver powder of Merc Dosage was commenced at 1 gm. of liver powder and was increased to 25 gm. Perhaps the technique with the nutrient medium m be successful in affording good, easily digest ible preparations.

Clinical Diagnosis and Treatment of Pituitary Disturbance of Growth. — Lucke. (*Klin. Wochenschr.*, viii, 1476, 1929.)

The condition of primordial dwarfism, which the individual is born abnormall small, is contrasted with the condition o

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pituitary dwarfism which exists when, in early childhood, in a previously normal individual, the function of the anterior lobe of the pituitary is impaired. In the ensuing disturbance of the growth process the bones show the first evidence. The development of the genitals remains stationary and involution does not take place. The state of the genitals accords with the other somatic development. True anterior lobe insufficiency shows itself in the arrest of development of normal intelligence in children. In very severe impairment pituitary cachexia occurs, an indication that, in older individuals, is the only evidence of the late appearing pituitary disturbance. The pituitary dwarf presents regularly an abnormal length of members with nether length and width in excess over the aggregate length. This state appears secondarily in the tardy development of the genitals. Fundamentally, the specific-dynamic albumin reaction and the blood sugar concentration are lowered. Often an eosinophilia is found in the blood. Changes in the sella turcica are seldom evident. As long as the ossification of the epiphysis has not taken place a year's treatment with substance from the anterior lobe of the pituitary can effect results, so that growth is noticeably improved and in females as further evidence of the efficacy of the therapy in an individual approaching puberty, the menses regularly ensue.

The Influence of Treatment with Spleen Extract on Lupus Vulgaris. — Artur Mahlo. (*Med. Welt*, iii, 971, 1929.)

On the basis of reports of Fliegel and Blayle concerning the healing of tuberculosis of the bone by the administration of raw spleen, the author treated three patients who had suffered for 15 to 19 years with lupus vulgaris, with spleen extract. Of this preparation of spleen (1 tablespoon is equivalent to 100 gm. fresh spleen) the patients were daily given 1 tablespoonful. Extensive improvement was evident locally as well as in respect to the general condition.

Concerning the Pathogenesis of Serious Conditions of Suprarenal Insufficiency. — G. Marañón. (*Presse méd.*, xxxvii, 1021, 1929.)

Among the instantaneous consequences of severe cases of the disease, the author mentions acidosis as a weighty one, if not the only one. Swingle stresses the fact that hypoglycemia and acidosis are both responsible, and the latter mainly is involved through inorganic sulphate and phosphate. Viale and Bruno rank among the factors the definite increase of blood viscosity (caused not by the loss of water but of plasma) and the radical conversion in lipoid metabolism. Likewise in all the worst forms of morbus Addisoni acidosis must be reckoned with before anything else, and therefore the author undertook treatment. He gave a diet rich in carbohydrates, followed by small insulin doses (5 units) with the addition of glucose (25 gm. in solution) three to four times a day, and next, alkali medication and caffeine.

Infantile Diabetes Treated for 5 Years with Insulin. — Mouriquand, Sedaillian and Mestrallet. (*Presse méd.*, xxxvii, 963, 1929.)

The authors present the case of a child who had lived in the hospital for 5 years and who, during this time, had been continually treated with insulin, in daily doses of 60-100 units. The child led a normal life and did not have a very strict diet regime. The urine eliminated amounted to 2-3 liters during 24 hours with a sugar content of 124.98 gm. and a blood sugar content of 5 gm. per liter. Its alkali reserve is good.

Concerning Intracardiac Injections of Adrenalin in Anesthetic Syncopes. — Perrin. (*Presse méd.*, xxxvii, 949, 1929.)

The author attempted the above mentioned method three times and concluded that as preliminary treatment it can be very efficacious. Everything must be ready in the operating room in order to give an intracardial adrenalin injection at a moment's notice.

Discussion:

P. Bertrand reported three cases of resuscitation of the heart with intracardial injection and Cotte reports of noticeable indirect results, so that he had to desist and he deemed it necessary to substitute another cardiac tonic with longer delayed activity. Chalier is skeptical concerning the above mentioned process, while Villard reports very successful results.

Rectal Treatment of Pernicious Anemia with Liver. — Hans Pulver. (*Therap. Gegenw.*, lxx, 294, 1929.)

In four cases of pernicious anemia very good results were obtained by the adminis-

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tration of liver through the rectum (hepatic powder with a liver value of 1:5 and 1:100). The compatibility for liver enemas and suppositories is on the whole good. Only in singular cases, in old people do complaints arise. Also in one patient the enema met with failure as it caused diarrhea and pains. A really successful liver therapy requires a very large amount of liver before a normal blood value is approximated or attained. Only then can one seek to preserve the remission with small quantities.

Further Researches on the Cardiac Hormone. The Action of the "Substances Actives." — R. Riegler and F. Tiemann. (*Pflügers Arch. ges. Physiol.*, ccxxii, 450, 1929.)

The authors could not corroborate the findings of Demoors and his collaborators who had reported that the "substances actives" derived from the Kieth-Flack nodes are the agents of automatism and as such are transmissible to the deficient or non-automatic activity of the heart parts, such as the isolated left auricle. The principle agent of the activity which was called "substances actives" is a non-specific substance existing throughout the organism, apparently belonging to the histamine group.

Experiments with the Problem of Pituitary Diabetes. — K. Velhagen. (*Klin. Wochenschr.*, viii, 1577, 1929.)

From the experiments of this author it follows that even with amounts of posterior pituitary hormone which have no physiological value, experimental evidence cannot be obtained that the blood sugar is a simple function of the proportion of the posterior pituitary hormone and insulin in the organism, and that it is not possible to induce a true case of diabetes by means of large doses of highly active posterior pituitary.

Concerning the Action of Kidney Extract on the Function of Contracted Kidney. — K. Stejskal. (*Klin. Wochenschr.*, viii, 1517, 1929.)

In seven cases of primary and secondary contraction of the kidney, decrease in blood pressure could be obtained by the intracutaneous injection of kidney extract and also of lipoid extract of the kidney. This action fails in genuine high blood pressure.

Discussion: E. Freund who obtained the extract added some general remarks to the report which culminated in the noteworthy complaint that students of internal medicine for the last ten years have had no interest in pathological chemistry.

L. Moszkowicz recalled the researches of Henschel in Basel, who with the aid of autolysates of various organs was able to create a specific action on the related tissue.

F. Necker was in doubt about the specific action.

E. Urbach reported on the intoxicating action of skin extracts.

On the Biology of the Placenta. — Rodekurt. (*Zentr. Gynäkol.*, liii, 1801, 1929.)

In two cases of hyperemesis a satisfactory result was obtained with treatment with placenta extract, in one instance a very marked success. Daily, 1-2 cc. was given intramuscularly (1 cc. equals 25 units). In three normal cases the influence of placenta extract was tested for the calcium and potassium content of the blood serum. The calcium content was always increased, in two cases likewise the potassium content. Follicellin to the amount of 8 units injected intravenously also gave after 6 hours a total calcium and potassium increase in the blood serum. Intracutaneous injection of this placenta extract as well as of total ovarian hormone, testifortan, thyroid gland oil, insulin, etc., gave no standard results.

Concerning Spleen Diet in Tuberculosis Patients. — P. Rüttgers and A. Kamsler. (*Beitr. Klin. Tuberc.*, lxxii, 1929.)

The patients were given daily to eat 100 to 150 gm. spleen mostly in the raw state; the method chosen for administration was, for the most part, in the form of beefsteaks, lightly roasted on the outside and inside rare. In patients who did not tolerate this method of treatment doses of pulverized spleen extract (analogous to prepared liver extract) were administered. This diet was tested on 12 patients. Subjective improvement was evident in the greater number of cases. The temperature decreased, coughing and expectoration diminished. A falling off of the bacilli in the sputum was fairly constant. The often observed rise in hemoglobin content of the erythrocytes is important except that high mountain air had earlier induced a change

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in this respect. There was a favorable influence in the physical condition of the most severe cases also. The murmurs were drier; radiologically, the primary exudative foci showed progressively less productive character; in contrast, the cavities appeared the least influenced.

Constitutional Weaknesses of the Cardiovascular System in Young Children. II.—L. Doxiades. (*Ergebn. inn. Med. u. Kinderheilk.*, **35** : 98, 1929.) **Constitutional Weaknesses of the Cardiovascular System and Internal Secretion of Young Children. IV.** — (*Ibid.*, 140.)

Schittenhelm and Eisler have observed in healthy persons, after intravenous or *per os* administration of thyroxin a rise of respiratory metabolism and an acceleration of albumin metabolism. The blood undergoes a decrease in content of Ca : K. The hydrogen ion concentration experiences no characteristic change. In one patient in whom edema had occurred in the climacterium, total rapid disappearance of the skin symptoms followed treatment with thyroxin. The size of the heart was definitely reduced and the electrocardiogram was normal.

Relatively little is known concerning the fate of the thyroxin introduced into the organism. The oxidative processes increased by the thyroxin, above all, serve the reconstruction process in muscular activity (convalescence) in growth and development. Thyroxin serves the vegetative system and its action evidently lies in the regulation of the fixed equilibrium within the system. There is a report of earlier date concerning the action of thyroxin on the vessels of the heart. Thyroxin evidently produces a change in the permeability of the capillary endothelium, acting either directly from the blood or tissues, or indirectly, following the rise of the oxidative processes. In myxedema there is, evidently in consequence of the lack of thyroxin in the blood and tissues, a decrease of permeability of capillary walls with consecutive dilation of the venous ends of the capillaries, the venous subpapillary plexus and hyaline changes in the cells of the corium.

The author reports the case of a 9 year old girl with congenital athyrosis, who had been under observation since the 8th year. With the institution of thyroid gland therapy (thyroidin, 0.1, three times daily) in addition to improvement of the other disease symptoms, there occurred a favorable influence on the cardiovascular weakness. After 3 months of continuous treatment with thyroidin, the child showed splendid general condition. The consequent year of treatment with thyroid gland was successful in remedying the whole myxedema symptom. Today we trend away from treating myxedema operatively — through the transplantation of the thyroid. The oral administration of an organ preparation now is the best choice of method. The thyroid activity is regarded as specific, dependent upon the peculiarity of the iodin-albumin linkage in the substance. Exact dosage of the preparation is hardly possible. For chronic hormone treatment the author recommends the *per os* method; because of the possibility of appearance of additional symptoms, the intravenous method should be avoided in polyclinical patients. In mongolism thyroid gland treatment does not accomplish the same as in congenital myxedema.

Hydrops Articulorum. — O. Fellner. (*Med. Klin.*, xxv, 746, 1929.)

The author treated many patients who suffered from post-climacteric pains in the joints with placenta extract and good results were always registered. Preparations containing albumin were never utilized. In placenta therapy of hydrops articulorum intermittens it is certainly not a question of unspecific therapeutic effect, but rather one of hormone influence.

Concerning the Various Actions of Histamin and Adrenalin on the Blood Vessels in the Rabbit's Ear. — E. Flatow. (*Arch. exp. Path. u. Pharmakol.*, cxli, 161, 1929.)

Small quantities of adrenalin do not produce the same effect on the blood vessels in the rabbit's ear as similar treatment with histamin does. In intravenous injection adrenalin acts in opposition to histamin in concentrations which will contract the blood vessels in the rabbit's ear.

Circulatory Problems. — Frey. (*Med. Welt*, iii, 611, 1929.)

A hormone of the circulation is found in the urine and blood. The isolated hormone was injected intramuscularly into patients afflicted with angiospasm, twice daily, in small doses. The author presents a female patient who was quickly relieved of the angio-

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spastic symptoms in the hands, objective cyanosis, subjective tingling, after the injection. The hormone failed to elicit results only in a case of long-standing circulatory defect. In hypertonics the hormone treatment also achieved noticeable improvement, and progressive muscular atrophy was likewise favorably influenced by the injection of this new circulatory hormone.

Therapeutic Application of the Hormone of the Circulation. — E. K. Frey. (*Münch. med. Wochenschr.*, lxxvi, 814, 1929.)

The report of a female patient who had been successfully treated with injections of the hormone of the circulation. Relaxation of the angiospastic condition of the legs could be observed. In four patients with intermittent lameness a dose of 1/20 mg. for several weeks, given twice daily was sufficient to capacitate the patient. The action on hypertonics was good and in two cases of angina pectoris the coronary arteries were capable of being influenced.

Embolism and Thrombosis. — Fründ. (*Med. Welt*, iii, 610, 1929.)

Doses of thyroidin seem to have induced a suppression of post-operative thrombosis and embolism. The administration of thyroidin appears to be of real import and to have an influence on the composition of the blood and thence influences the coagulum. Reference was made to the rarity of thrombosis and embolism following goiter and Basedow operations.

Concerning the Relationship of Pituitary Gland and Hypothalamus to the Retention of Water. — E. Frank. (*Med. Klin.*, xxv, 679, 1929.)

The clinician who studies the action of substance from the posterior lobe of the pituitary gland in healthy persons and in those patients afflicted with retention of urine must come to the conclusion that there is involved here an incretion. The diuretic effect of the extract is not its natural capacity, but rather it enters if the pituitary substance is administered to narcotized animals or is introduced directly into the blood vessels. With the slow penetration after subcutaneous injection, there is always found in human beings and also in experimental animals, an inhibition of water diuresis. The powerful action of small quantities of pituitary substance on the retention of water in normal individuals is very evident in Vollhardt's water experiments.

If one administers at regular intervals, about every 3-4 hours, to patients suffering from diabetes insipidus, a subcutaneous injection of 1 cc. of an active extract, the patient is kept healthy as long as treatment lasts. The 24 hour urine output is immediately reduced from 10 L. to 1½ L. and under. Gorke observed in one case, on 3 test days, as much as 12 hours of anuria. The specific gravity of the urine rose extraordinarily.

Because of the knowledge that the substance from the tuber cinereum is an incretion carrier as well as an incretion storehouse, and that a vicarious, hypertrophic portion of the incretion organ is inseparably allied with it, the demonstrative force of the argument presented in favor of the existence of an isolated center of water control and with it the experimental evidence that diabetes insipidus rests upon an affectation of the nervous element at the base of the mid-brain is destroyed; the true endocrine origin of the disease is well established.

Folliculin, Insulin and Diabetes. — F. Rathery and M. Rudolf. (*Bull. et mem. soc. med. hôp. Paris*, **44** : 741, 1928.)

The cessation of menorrhagic hemorrhages was observed following injection of folliculin in some cases. In two cases of severe diabetes in women a combined treatment with insulin and folliculin injections had as result a decrease of urinary sugar, disappearance of acetone and oxybutyric acid excretion. In one of the two patients the doubled folliculin dose had the opposite effect. In an 11 year old girl, who had not yet menstruated, glycemia was increased through the combined insulin-folliculin medication.

The Basal Metabolism. — P. Liebesny. (*Wien. med. Wochenschr.*, **78** : 1247, 1928.)

The clinical significance of the determination of basal metabolism is dependent upon the information obtained thereby concerning the function of the thyroid. B. R. Hill has shown that in 54 cases in which no typical symptoms of myxedema existed but only disturbances of circulation, the basal metabolism fell to about 13-47 per cent below normal. Thyroid therapy effected cure in 12 cases, improvement in 38 cases and left only 4 cases uninfluenced. Eppinger showed that in some

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cases of edema, which had remained refractory to every therapy, the administration of thyroid tablets proved to be the best diuretic. This by no means indifferent therapy will be resolved upon all the more readily in such cases when the determination of the basal metabolism gives strict indication for it. Eppinger also showed that individuals with normal kidneys present an accelerated chloride metabolism with the feeding of thyroid substance and finds moreover that patients with exophthalmic goiter show a rapid excretion of sodium chloride whereas myxedema patients retain sodium chloride. Through the determination of basal metabolism it can also be determined whether it is a question of an exogenous or endogenous obesity and when in addition the investigation of the specific dynamic albumin action is added, one can decide whether this obesity is dependent upon functional disturbances of the thyroid, pituitary or sex glands and thus hit upon the proper therapeutic measures.

Relations between the Digestive Tract and Blood Diseases. — Laqueur. (*Med. Welt*, 2 : 1538, 1928.)

In Holland good results were obtained in pernicious anemia by treatment with liver and liver extract prepared according to the instructions of the Committee for Pernicious Anemia (U. S. A.). Liver therapy is also to be tried in secondary anemias when other therapeutic measures remain without success. 1.0-1.5 gm. of the liver extract used corresponded to 100 gm. fresh liver. In most cases 3, 4 or 5 gm. of the liver extract suffice, but 12-15 gm. may also be given. The attempts at biological standardization of liver preparations have until now been without success.

The Internal Secretion of the Salivary Glands. — Goljanitzki. (*Ergebn. ges. Med.*, xiii, 125, 1929.)

In earlier experiments the author determined the following facts. Besides the production of secretion the salivary glands also have an endocrine function. The characteristic influence of the salivary gland incretion is on the condition of nutrition. In young animals the salivary glands have an important influence on the growth of the animal. Galebski tested the problem of endocrine function of the parotid gland and found that the fluid derived from the parotid according to the method of Krawkow, is physiologically active, as is evident from the reaction on the blood vessels of the isolated rabbit ear and from tests on isolated rabbit and cat heart. On the isolated heart of these animals the fluid effects an inhibitory action for the most part. In five of six cases intravenous injection called forth a decrease in blood sugar that paralleled the amount of injected fluid.

These facts are evidence, therefore, that the parotid presents, besides an excretory function, a substance which acts on the individual organ as well as on the entire organism.

Endocrinology and Opotherapy. — G. Hallion and R. Gayet. (*Monde méd.*, xxxix, 411, 1929.)

From a general consideration of the administration of organ preparations in the clinic, the author reports, after mention of numerous contributions to the literature, concerning the administration of the following organ preparations: Liver, insulin, pituitary, suprarenal, thyroid gland, parathyroid gland and mammary gland. In an ensuing resume the diseases were enumerated in which organ preparations were administered with important or insignificant results. These are asthma, Basedow, cancer, diabetes, diphtheria, hemoptysis, cardiac neurosis, edema, insomnia and tuberculosis. For all these diseases the preparations used, the experiments and the results obtained were presented.

Skin and Venereal Diseases. — Max Joseph. (*Jahresk. ärztl. Fortbild.*, xx, 14, Skin Diseases, page 20, 1929.)

Pulvermacher presented the question whether the skin is an organ of internal secretion. Theoretically it is possible that the skin produces one of the parasympathetic tonic hormones and acts as a synergist with the suprarenal cortex, with which in this particular sense it is comparable.

Concerning the Rôle of Adrenalin, of Insulin and Glycogen Sugar on the Mechanism of Attacks of Angina Pectoris. — J. G. Katz. (*Fortschr. Med.*, xlvii, 303, 1929.)

Hetenyi worked with two cases of diabetes and cardiac sclerosis in which at the conclusion of every injection of insulin attacks of angina pectoris occurred, which were regularly excluded, however, if the patient

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received sugar simultaneously with the insulin. Strauss does not believe that direct injurious action of insulin takes place in the heart.

Chasanoff believes that the glucose contains a nutritive substance for the heart muscle. A series of experiments and clinical observations has shown that adrenalin and insulin are to be regarded as antagonists. The adrenalin circulating in the blood mobilizes the glycogen so as to transform it into glucose. Herter showed that intravenous injection of adrenalin induces glycosuria. Zuelzer determined that adrenalin glycosuria is excluded when insulin is administered simultaneously with the adrenalin. The chemical nature of insulin is not yet explained. Insulin acts not only on glucose, but also it incites changes in the metabolism of nitrogenous combinations, of fats and of lipoids. According to Krawkow, adrenalin distends the coronary arteries in the greater number of instances. Schwarzmann observed infallible antispastic activity of adrenalin in spastic condition of the heart. Some authors describe insulin as a vagotropic substance, others find a decrease in vagotonus and an abatement of spasmophilia through the use of insulin. Deicke reported on a case of angiospastic hemiplagia with motor aphasia, in which following the injection of 40 insulin units, hypoglycemic reaction occurred. The attack was renewed after two injections of 25 units, 6 hours after the second injection.

Concerning the Action of Post-Pituitary Extract on the Musculature of the Uterus. — Hermann Knaus. (*Zentr. Gynäkol.*, liii, 1162, 1929.)

The administration of pituitary extract to induce labor pains does not always produce the desired therapeutic effect. It is for example impossible, with the aid of pituitary extract to induce an abortion or to bring about premature birth. Therefore, it is quite inexplicable on what basis pituitary extract acts, for, before the normal termination of pregnancy, it can induce no labor symptoms or only impotent short ones.

Up to the present the explanation has been made that there is a weak sensibilization of the uterus for the activity of pituitary extract at this time of pregnancy. The processes which are concerned during all periods of pregnancy, during birth and the puerperium in the uterus, and which are significant for the reaction of pituitary extract can well be studied in the rabbit. In a well developed virgin animal, the tonus of the musculature of the uterus was markedly increased by pituitary extract. Intra partum, there occurs after the use of pituitary extract one of the most ideal forms of rhythmically increased contractility for the progress of delivery. (Curves.) Because of this property to release uniformly flowing waves of contraction, post pituitary extract is undoubtedly the best ecbolic. Twenty-four hours post partum the rabbit uterus is no longer capable of showing response to pituitary extract: the contractions analogous to those effected during the process of delivery. (Curve.) Forty days post partum a reaction similar to that in the infantile organ occurs after the use of pituitary extract. Depression of the muscular activity of the uterus is the base for the defective reaction to pituitary extract. Likewise the musculature of the uterus loses its power to react to extract of the post pituitary under the influence of corpus luteum.

Concerning the Influence of Administration of Thyroid Gland on Albumin and Fat Metabolism. — B. Kommerell. (*Biochem. Zeitschr.*, ccviii, 112, 1929.)

Two fasting experiments were undertaken on a dog in an interval of 5 weeks; during both fasting periods thyroid gland was fed. Representative of the action of feeding thyroid gland there occurred a basal metabolism rise of 30.5 per cent. This increased consumption of calories was defrayed on the average by 31.3 per cent albumin combustion and by 68.7 per cent fat combustion. The loss of body nitrogen during hunger, under thyroid gland activity reached almost double its original value.

The True Acidity in Isolated Portions of the Male Genital Apparatus of the Rat and Its Hormone Limitation. — Y. von Lanz. (*Pflügers Arch. ges. Physiol.*, ccxxii, 181, 1929.)

On the basis of his own observations the author determined that the true acidity in isolated portions of the male genital apparatus is not due to spermatogenesis, but rather to the existence of a generative gland substance in general. Bilateral castration differentiates the epithelium and determines the H-ion concentration of the secretion of this gland independently of the blood. The testicular

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hormone is active also after ligature of the ductuli efferentes. Apparently it was not absorbed in the epididymis.

Transplantation of Preserved Ovary. IV. Transplantation of Desiccated Ovary. — A. Lipschutz. (*Virchows Arch. path. Anat. u. Physiol.*, **272** : 245, 1929.)

Transplantation of totally desiccated ovary into the kidney of castrated male guinea pigs is always ineffective. By grafting ovary not completely desiccated, endocrine activity of the mammary gland apparatus occurs, which can become so intense that milk is formed. The endocrine action lies in a new formation of hormone in the grafted material in the organ of the host animal. Microscopic examination shows that the organ presents follicular development. The preceding damage to the organ does not inhibit the endocrine activity.

Investigations on the Origin of Creatin or Creatinin in the Animal Organism. — E. Abderhalden and S. Buadze. (*Zeitschr. ges. exp. Med.*, lxv, 1, 1929.)

As a result of the observations of various authors who, by the administration of thyroid gland substance induced evidences of creatin or creatinin, a test was made to determine whether the addition of thyroxin to muscle broth to which guanin had been added would influence the formation of creatin or creatinin. Hence it was evident that thyroid gland incretion caused the formation of creatinin and only without the addition of guanin.

Experimental Investigations on Corpus Luteum. — L. Brouha and H. Simonnet. (*Presse méd.*, xxxvii, 591, 1929.)

Corpus luteum extract, injected into normal female rats causes the suppression of the estrous cycle, provided the dosage is large enough. The genital tract assumes an appearance similar to that observed in castrated animals. With smaller doses a condition is established suggestive of a pseudo-abortion, without the characteristic estrus, but with the development of the uterus. With weak doses extention of the period of estrus only is obtained. In sexually immature animals the extract preserves the first estrus. In castrated animals no development occurs either in the uterus or in the sex glands. The extracts act on the estrous phenomena evidently in such a manner as to suppress the production of folliculin, but not its activity, for if folliculin and corpus luteum extracts are simultaneously injected the latter does not prevent the action of folliculin.

Hormone of the Anterior Lobe of Pituitary as Related to the Male Genital Tract. — L. Brouha and H. Simmonet. (*Presse méd.*, xxxvii, 591, 1929.)

Daily intramuscular implantation of portions of the anterior lobe of the pituitary show that this gland exercises a remarkable stimulating action on the male genital tract (rat, mouse). The activity of the anterior pituitary extract varies with the method of preparation and often with the dose administered. If the active principle which is contained in the urine of women at the beginning of pregnancy is used, there may be regularly observed a striking change in the genital tract of sexually immature animals, similar to that in adults. With extract of anterior pituitary prepared by alkaline method a definite development is obtained when small doses are employed and in contrast, an intensification or a retrogression with larger doses. We do not yet know whether this activity is referable to two antagonistic substances, or to a single substance which is active variously when injected.

The Zondek-Aschheim Pregnancy Reaction. — R. Brühl. (*Deut. med. Wochenschr.*, lv, 696, 1929.)

1. A positive result with the pregnancy reaction of Aschheim and Zondek gives very definite evidence of pregnancy. The negative result of the reaction excludes pregnancy with 100 per cent surety.

2. It is very evident that in the anterior lobe of the pituitary gland at least two hormones are formed. The one effects maturation of the follicles and is found usually in the urine of climacteric and castrated females, the other influences the formation of corpus luteum and is especially evident in pregnancy.

3. The hormone could not be demonstrated in the urine of mares in foal or cows with calf.

Organ Extracts in Their Action on Immuno-Biological Processes. — Pockels. (*Münch. med. Wochenschr.*, **76** : 770, 1929.)

Animals difficult to immunize were made good producers of antibodies by the injection

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of spleen extract. Spleen and lung extracts were administered orally to human beings in order to determine the active di-immunization. A specific influence was derived.

Insulin and Nutrition Depots. — A. Löw and A. Krčma. (*Biochem. Zeitschr.*, **206** : 360, 1929.)

The author studied the problem of how insulin, administered under various conditions affects the carbohydrate capacity of fat. The mouse served as the experimental animal.

The experiments show that a marked lessening of liver carbohydrate is induced after insulin injection. The beginning of the decrease can be determined 1½ hours after the injection. The decrease in liver glycogen is to be accounted as a direct action of insulin. In fatty tissue only inconsequential changes of carbohydrate content could be observed. The contrast with the action on liver tissue is important. It proves that insulin acts differently on fatty tissue as compared with the liver. The observations made at that time, namely that in fasting rats, more glycogen was found in the fatty tissue than in normal animals, permits the conclusion that carbohydrate can also be formed in the fatty tissue. The experiments of the author make it evident that the lobule organ can claim this function.

Concerning the Treatment of Milk Retention. — Walter Mestitz. (*Münch. med. Wochenschr.*, **76** : 782, 1921.)

The painful retention of milk, especially in sensitive women, must be actively combated. In this case diuretics are useful. Because thyroidin is a good diuretic, Kraul gave thyroid gland substance as treatment for milk retention and obtained good results.

Cell Formers and Cell Forms of the Blood. I. Changes in the Blood Formers during Complete Cure of a Granulocytosis. — W. Stockinger. (*Zeitschr. ges. exp. Med.*, **65** : 27, 1929.)

The author was able to determine that in granulocytosis, adrenalin acted to cause an increase of cells in the blood. The less this is, the worse off the general condition of defense in the organism. The cell increase after adrenalin is effected by the entrance of large unformed cell elements into the blood circulation.

Further Investigations on the Relationship between the Pituitary and the Ovum with Its Accessory Glands. — Hermann Siegmund. (*Münch. med. Wochenschr.*, **76** : 776, 1929.)

Following the implantation of rather large amounts of anterior pituitary tissue into infantile female mice, there appeared evidences of premature estrus due to the premature mobilization of hormone incretion in the ovary. After the implantation corresponding to high dosage it is even possible in the pregnant mouse to arouse the latent follicle of the ovary in pregnant state and cause proliferation and luteinization of the follicle cells. However, it is not possible to demonstrate estrus symptoms in the vagina during pregnancy neither could the ovary be forced experimentally to further incretion by the administration of anterior pituitary incretion. The release of the excretory function of the ovary, *i. e.*, the evacuation of ripe ova, could not be ascertained by the author. The researches performed according to various physiological methods all speak for the inhibition of each ovulation during the time of function of the corpora lutea. The author reports that the pregnancy test of Aschheim is exclusively reliable. Many contributions deny the control of the sexual function by the pituitary; the more prevalent perception that the ovum and its accessory glands have an active effect on the expiration of sexual function must be correct.

Hydrops Articulorum Intermittens. — H. Schlesinger. (*Med. Klin.*, **25** : 746, 1929.)

Many authors report that the therapeutic reaction in hydrops articulorum intermittens is unimportant. As may be seen from the literature, the disease is associated with the function of the female genitals. It occurs after prolonged puberty or after lactation in an abortion or parturition. The author applied therapeutics to this etiological association, and treated the patient described with placenta extract, throughout 5 months one injection every second day. The swelling was lessened, it did not last very long and it was no longer painful. The interval between attacks, which formerly was 8 days long, now was 12 days. The author believes that still better therapeutic effects may be obtained by the administration of stronger extracts — those given were quite weak.

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Text Book Opinion

"The opposers of the oral method must remember that it will not produce the immediate and dramatic result that injection produces but then it does not expose the patient to the dangers of hypoglycaemic reactions nor the increasing dread of the needle."

(W. M. Crofton, *An Outline of Endocrinology*, 1929.)

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Test of Insulin-Induced Hyper-Hypoglycemia in Normal Subjects and in Pathological Syndromes (Emaciation, Obesity, Diabetes). — F. Moutier and L. Camus. (*Arch. mal. app. dig. et mal. nutrit.*, 19 : 297, 1929.)

The matter taken up in this article concerns a combination of a hyperglycemic and a hypoglycemic process an assumption depending on the hypoglycemic reaction of one person. However, one can not draw unconditional conclusions from work on emaciated individuals; indeed several of the thin persons observed by the author reacted strongly to the insulin test and presented quite variable results when insulin was given in therapeutic feeding. In any case it is determined that the test never did the thin people any harm. Hypoglycemic symptoms occurred only in persons with intense bulimia. Patients with dysthyreosis and some with sympathicotonic symptoms reacted quite easily. The test is also valuable for the comparison of the activity of insulin preparations of various origin.

Contributions to the Study of the Importance of Blood Glands for the Digestive Tract. The Action of Adrenalin and Insulin on the Secretion of the Succus Entericus. — B. A. Schazillo. (*Arch. Verdauungskrankh.*, 45 : 264, 1929.)

It has long been known by the clinician that the patient with hypothyrosis suffers from obstipation and the patient with hyperthyrosis suffers from diarrhea. Marbé, after feeding dogs with thyroid gland, observed a rise of intestinal secretion. The study of the action of adrenalin and insulin on the secretory function of the intestine has not only a theoretical interest, but also a great practical interest. The author undertook investigations on this problem, and found:

1. That the irritating action of subcutaneous injection of adrenalin — particularly at the height of digestion — is not favorable to digestion after meat extracts have been consumed. One gains the impression, therefore, that in this case the irritation is caused by an irritating substance produced by the intravenous injection of the incretion medium. Adrenalin in subcutaneous injection increases the activity of the sympathetic nerve element in the organs. At the culmination of digestion, however, the same quantity

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of adrenalin can increase the irritating effect on the animal only when given intravenously.

2. The irritating action of small doses of insulin on dogs is elucidated; on the basis of the investigation, it is to be assumed that the secretory process of the intestine was influenced both by adrenalin and by insulin. Insulin arouses the intestinal secretion in fasting dogs as well as at the culmination of digestion.

Influence of Internal Secretion on Dermographism. — G. P. Sanna. (*Med. Welt*, **3** : 530, 1929.)

The author has studied the variation in color, the time of appearance and the duration of dermographism in persons to whom had been given a high dosage of various internal secretion substances. Thyroid gland, suprarenal, pituitary, testicular and ovarian substance were administered *per os*. One hundred individuals were tested, of whom twenty served as controls.

Ovarian preparations (extract of the generative glands of lower vertebrates) brought out red, superficial dermographism with significant lessening of time of appearance and disappearance as well as the entire duration of the symptom itself. Besides the reaction was very intense: reflex dermographism.

Male generative glands (testicular extract of lower vertebrates) gave almost the same symptoms.

Thyroid gland preparations called forth a very pronounced, superficial, red dermographism, often accompanied with lateral white streaks, with definite lengthening of the time of onset and disappearance of the symptoms and great increase in the duration. The degree of severity was somewhat diminished.

The same symptoms were called forth by entire suprarenal extract, but the reaction was stronger, and more easily provoked.

With pituitary extract no definite action on dermographism was obtained.

The Functional Significance of Isolated Portions of Pituitary Gland. — A. Biedl. (*Endokrinologie*, iii, 241, 1929.)

On the basis of numerous observations it is now a well known fact that the anterior lobe of the pituitary contains a hormone capable of effecting the maturation of the sex glands. With consideration of the information that, in mice, the administration of large quantities of anterior pituitary hormone causes complete luteinization of the ovar... overdosage in the form of a single large appl... cation of mouse units rather than long-or... tinued parenteral application of anteri... pituitary hormone is to be guarded against. Whether the anterior lobe incretion has any relation to the carbohydrate metabolism incidentally has not yet been determined in this instance.

The pars intermedia of the pituitary with the help of its incretion influences the requirement and consumption of substances, the general variations, the constancy of body heat, as well as the activity of isolated vegetative organs. The extensive information which we have gathered concerning the action of the extracts of the pars intermedia and posterior lobe gives evidence of the metabolic action of these parts of the pituitary. The question of where this active substance originates is not argued, nor is its hormonal nature generally acknowledged. Kamm and his colleague have shown that in pituitrin there is not a question of a single substance, but rather of several substances. The substances possessing either promoting or inhibiting activity on diuresis, according to existing conditions, seem to be contained in the fraction with pressor activity. The fat metabolism was influenced in such a way that after administration of pituitrin there occurred a considerable falling off of fat in the blood and a lessening of the ketone bodies.

The pituitary incretion acting on the center of vegetative metabolism can interfere indirectly in the function of the animal nervous system.

. The pars nervosa and the adjoining stalk were found to have no incretory significance.

The functional significance of the pars tuberalis is not explained.

Endocrine Disturbances in Childhood — Rudolf Neurath. (*Wien. klin. Wochenschr.*, **42** : 617, 1929.)

In the last stages of embryo life and soon after birth a definite overweight of the s... glands and cortex of the suprarenals occurs that is evident in the anatomical size and in the quality of the skin and hair. Besides the intensified growth of the sex glands an increase in metabolism, due to unusual increase in hyperactivity of the thyroid gland, is characteristic for puberty; growth in height at this period is fostered by the anterior lobe of the pituitary. In adolescence the s...

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glands attain prominence; metabolism is undertaken by the hormone of the thyroid gland and the adrenal system and the lobule apparatus of the pancreas become more and more important for consumption and metabolism. Congenital thyroid gland defect is evident in the characteristic symptom of myxedema. In children this form is developed soon after birth.

There are also constitutionally hypothyroid individuals who have great need for hormone or whose thyroid gland functional capacity is greatly lowered — torpid adipose persons with lowered basal metabolism.

Also the temporary hyperthyroidism producing obstipation in newborn infants, which is always associated with the obstipation of the nursing mother, must be mentioned. The treatment of sluggishness of the bowels in both mother and child is promptly effected by thyroidin. In no phase of endocrine disease has substitution therapy acted so extraordinarily and showed its efficacy as in the treatment of hypothyroidism and athyrosis. Substitution therapy is accomplished by the ever increasing improvement of production of the hormone of the thyroid gland. As a daily dosage for nurslings thyroidin was given in tablet form of 0.1 gm., older children were given as much as 0.3 gm. The action of the hormone on the physical symptoms as well as on the psychic deficiencies is important. The endocrine function of the suprarenals is twofold. Recently, E. Schwarz performed investigations from the viewpoint of modern embryological opinions to shed light on the problem of interrenalism. In order to bring out all the evidences of interrenal syndrome depending on suprarenal hypertrophy, we have only to admit that the excessive activity of the suprarenals on the sex-determining gene complex of the chromosomes is such that the factor bound to the X-chromosome is impaired either by its own mitigation or by that of its opposing medium. Accordingly, the zygotic sex-determination is capable of being influenced by hormones.

Method of Increasing and Decreasing Secretion of Milk at Parturition. — Michel Wachtel. (*Zentr. Gynäkol.*, **53** : 987, 1929.)

The attempt to cut off as quickly as possible an existing milk secretion, or not to "allow" the milk secretion to occur, is important in cases of intrauterine death of the fetus; further in women who have suffered a miscarriage in the later months of pregnancy, or whose offspring has died soon after birth. The congestion and tension of the breast full of milk is very painful to women. The treatment of this uncomfortable condition is most easily and simply effected by thyroidin. The earlier torment inflicted, of having the women go thirsty or to stem the function of the mammary glands by purgatives has become superfluous. After the administration of thyroidin, besides greater permeability of the tissues and influence on the osmotic oncotic pressure, there occurs a dispergence of the white blood corpuscles, for the increase of albumin and the decrease of globulin and fibrin. The result, therefore (Starlinger) is a much augmented capacity for swelling and a greater power to take up water. Kraul mentions the fact that he gave this thyroid gland preparation too, in painful condition of the breast during menses and obtained results. The author reports on twenty women to whom he gave early in the day and in the evening, 1 thyroidin tablet 0.3 and at midday he supplemented this treatment with 1 tablet of diuretin 0.5 gr. The treatment was continued for 3 days. Milk secretion did not occur at all. No harmful consequences have ever occurred.

Communications on the Activation of Adrenalin by Thyroxin. — T. Zimmermann. (*Biochem. Zeitschr.*, **206** : 369, 1929.)

The author undertook investigations to determine whether the activity of adrenalin could be influenced by the secretion of the thyroid gland. Following this the decrease of the glycogen content of the musculature after adrenalin injection was determined, and then the action of similar doses of adrenalin was noted after a thyroxin injection had been made. From all these tests it was learned how variable is the action of adrenalin. After adrenalin 1:10,000 there was a decrease of 21.8 per cent; with adrenalin 1:1000 this was found to be 25.28 per cent. The glycogen content of the liver with adrenalin 1:10,000 amounted to 1.79 per cent (resp. 2.16 per cent) with adrenalin 1:1000, 0.90 per cent.

If adrenalin injection is made 6 hours after a thyroxin injection, the diminution of glycogen in the muscle amounts to 37.6 per cent, the liver glycogen dropped to 0.257 per cent. Hence upon consideration of the

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thyroxin alone it follows that the thyroxin increases the activity of adrenalin for carbohydrate metabolism.

A Case of Cryptogenic Pernicious Anemia Which Proved Refractory to Simple As Well As Combined Liver Therapy.—Emile Weil. (*Paris Med.*, **19** : 416, 1929.)

Report on a case of cryptogenic pernicious anemia diagnosed as such clinically as well as by post-mortem examination. The patient, who had shown a remarkable improvement throughout a month of combined liver and insulin therapy, a few weeks later suffered a relapse and became entirely refractory in this stage to liver-insulin therapy. The author emphasizes the fact that too little observation has been made on those cases resistant to liver therapy, and he was supported in this opinion by Fiessinger and Tixier.

Severe Hemorrhage after Delivery. Non-Operative Treatment. Cure.—Voron and Pigeaud. (*Bull. Soc. obstet. et gynecol. Paris*, No. 3 : 225, 1929.)

In a 21 year old primipara, 2 days after spontaneous delivery, there occurred rise in temperature with chills and on the 10th day severe hemorrhage, which ultimately assumed a menacing aspect and made remedial measures necessary. The patient received only ergotin injections. Then, because the pulse became worse and further, anemic symptoms appeared, the patient was given injections of pituitary besides the ergotin injections, whereupon the hemorrhage was at once diminished, despite the noxa of a transport for eventual hysterectomy, and was entirely stopped within 23 hours by repeated pituitrin-ergotin injections.

Concerning the Relationship between Psoriasis and Ovarian Function. — E. Vogt. (*Monatsschr. Geburtsh. u. Gynäkol.*, **31** : 385, 1929.)

The hormonal theory always plays an important rôle in the explanation of psoriasis. Since the theory of purely thymogenic origin is so disputed, it might appear that the thymus gland plays a part in conjunction with the sex glands. The author reports on four cases in which the relation between the origin of the skin disease and the activity of the female sex glands seems quite certain. Case 1 gave evidences three times of this skin disease which first appeared in the 12th year, before the beginning of the menses (which began in the 14th year); the second time, after the birth of the first child, when amenorrhea of lactation was present; the third time, soon after the commencement of the menopause. In the second case psoriasis occurred in the course of amenorrhea of lactation; in the third case, after roentgen amenorrhea in a 50 year old female patient; in the fourth case after operation, radically, of a myoma. Basch observed that the disease appeared after the physiological amenorrhea of pregnancy; Scheuer observed a pronounced aggravation of the symptoms during pregnancy. Practically, hormone substitution therapy with ovarian preparations is to be recommended in the treatment of psoriasis, the most protracted and severest of those diseases requiring treatment; it may be recommended all the more since effective, active ovarian preparations can now be prescribed, to be taken not only parenterally but also orally. Further it may be noted that psoriasis has been treated repeatedly with insulin and good results ensued. From this one can assume a purely endocrine action of the pancreas hormone. However, there can also be the matter of a vitamin effect, the insulin working as a vitamin agent. Indeed the pancreas hormone contains abundant amounts of vitamin D.

Concerning the International Standardization of Drugs. — L. E. Knaff. (*Wien. klin. Wochenschr.*, **41** : 1495, 1928.)

The Hygiene Organization of the League of Nations has suggested all the methods of standardization of drugs, also such as can be standardized by biological method. As regards pituitary extract, the Conference is of the opinion that the desiccated preparation of the posterior lobe of fresh pituitary prepared by acetone extraction, which has been proposed by Prof. Voegtlin at the Edinburgh Conference, is suitable to be accepted as international standard preparation. For the biological standardization of the oxytocic activity the test on the isolated uterus of the virginal guinea pig according to the Pharmacopoeia of the United States, 10th Edition, is recommended.

For the estimation of the action on the blood pressure comparative investigations on anesthetized dogs or on decapitated cats are recommended. For the determination of the antidiuretic action the test on the unanesthetized dog, on the healthy human being

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in patients with diabetes insipidus is regarded as suitable. The Commission is of the opinion that in the event of the antidiuretic action being due to a third substance, there is the possibility of expressing the activity in antidiuretic units of the same standard powder. Still further investigations are, however, necessary to establish the unity and strength of the standard preparations of the different firms with respect to their antidiuretic action. In all cases a unit should be that which corresponds to the action of 0.5 mg. of the standard powder.

As international standard preparation for insulin, the desiccated preparation of hydrochlorated insulin is recommended, which was established by a resolution of the Edinburgh Conference of the Medical Research Council of Great Britain. One mg. of this standard corresponds to 8 such insulin units (1 unit — 0.125 mg.) as were previously defined by the Insulin Committee of Toronto University. The appointment of a sub-committee is recommended which will submit proposals with regard to the permissible organic desiccated residue per unit and with regard to the testing of the strength.

With respect to thyroid preparations the Genoese Conference was of the opinion that the biological estimation of thyroid substance was not in general necessary, but the iodin content in specific union with the active substance can be considered as measure for the therapeutic value. In order to recognize any increase of artificial iodin content, for example with iodides, the estimation by the so-called acetonitril method (Reid Hunt and Straub) is proposed. As comparative standard for the biological testing a desiccated preparation from healthy thyroid with an iodin content of 0.2 per cent is recommended.



DYSMENORRHEA

A HOSPITAL REPORT

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Leiner's Dermatitis. — Szentléleky-Szász. (*Monatsschr. Kinderheilk.*, **40** : 362, 1928.)

In nurslings with exudative diathesis and in those who suffer from Leiner's dermatitis subcutaneous injection of ½ to 1 cc. posterior pituitary extract caused the skin to become very pale within a few seconds and the skin process often disappeared after 24 hours; at the latest, however, within 4 to 5 days. The more severe the skin changes the more intensive the pallor. In one case of Leiner's dermatitis, under the action of posterior pituitary extract, the liver swelling decreased in striking manner.

Better results were obtained with decrease of the dose. The more severe the process, the smaller the dosage; on the average 1/3 cc. twice daily, in all 4 to 5 injections. The edema which lasted for a long time with 1 cc., did not come into question with small doses. In severe eczema also favorable results were obtained with post-pituitary extract. J. Pilcher (Cleveland) gives subcutaneously or intramuscularly in eczema 1‰ extract of suprarenal to 0.1 to 0.3 cc., and obtains cessation of the itching.

Concerning the Question of the Decrease or Abolition of Labor Pains. — Hoehne. (*Zentr. Gynäkol.*, **52** : 2773, 1928.)

The slight degree of narcosis intoxication with ether or ethyl-chloride injures — in otherwise excellent execution — the activity of the labor pains on the bearing down process. For this reason the simultaneous intravenous injection of a pituitary preparation is important in such cases, and the substitution of Kristel's extraction for the lacking abdominal muscular pressure.

Insulin, Synthalin and Glukhorment. A Comparative Investigation concerning Their Action on Glucose Fixation through Cells. — E. B. Salen and T. Nyren. (*Acta med. scand.*, **69** : 69, 1928.)

Experiments with synthalin and glukhorment carried out under corresponding experimental conditions show an effect of increasing fixation of glucose for both these substances identical qualitatively with that of insulin. Under the supposition that glukhorment contains a substance identical with synthalin or closely related to it chemically, the assumption is justified that the effect of increasing glucose fixation observed is wholly conditioned through a synthalin-like substance present in the glukhorment. The experimental results of the authors support the opinion that the glucose fixation-increasing action of insulin is a specific insulin effect which also has an essential significance for the function of insulin *in vivo* (for its sugar-regulating function). The latest attempts to define insulin chemically (Abel and his associates) have led to results which speak rather for than against the assumption that the specifically active constituent of insulin can be a substance closely related to synthalin. The demonstration of a qualitatively identical action *in vitro* of all three substances is calculated to support still further the whole conception.

A Chemical Reaction to Vitamins and Hormones. — E. Christensen. (*Münch. med. Wochenschr.*, **75** : 1883, 1928.)

The extensive harmony between vitamins and hormones pointed out by E. Vogt, suggested the question whether hormones give the same color reaction as is obtained when vitamin-containing extracts are diluted with phosphoric pentoxide. Accordingly, preparations of ovary and testis were tested and in both the same reactions with phosphoric pentoxide were determined. Moreover, a large number of commercial insulin preparations were examined and it was found that all without exception gave a positive phosphoric pentoxide reaction, to be sure in very different strengths, which seems especially noteworthy. There came to light, therefore, with respect to the reactivity to phosphoric pentoxide, various differences between the individual brands of insulin, such as were earlier described concerning the albumin content. To what extent these differences parallel the therapeutic usefulness of the individual preparations must first be explained by further investigations.

Hypergenitalism and Macrogenitosomia. — Serdukoff. (*Rev. franç. endocrinol.*, **6** : 378, Oct., 1928.)

By hypergenitalism is meant the precocious appearance of puberty with the organism remaining in a state of infantile development. Cases of hypergenitalism are much less frequent than the various forms of insufficient development and hypofunction of the genital organs. In definite clinical cases the symptomatology of hypergenitalism or macrogenitosomia in women presents

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complex of primary or secondary symptoms translating the abnormal precocious development and premature manifestation of the functions of the genital glands. Almost always following precocious development of the genital organs, there occurs an exaggerated development of the whole body, muscles and skeleton. In relation to this exaggerated development, at the beginning, the attention is drawn by the tall stature and by a considerable weight.

Finally as the affection develops there is precocious ossification of the epiphyseal zones and the tendency to growth stops. The height, in general, in cases of hypergenitalism does not reach dimensions such as are observed in gigantism.

Hypergenitalism or macrogenitosomia is of endocrine origin. The height of girls suffering with macrogenitosomia exceeds by a third or a fifth that of their comrades; their weight may be double the normal. From the constitutional point of view one does not always find congenital factors of functional anomalies of the genital glands. Frequently girls suffering from this disease come from fertile families (nine, twelve and fifteen children) with twins and even triplets. The precocious appearance of menstruation is also found. At times familial hypergenitalism is observed.

The tendency to increase in size in the course of macrogenitosomia is also manifested for certain secondary sex characteristics: mammary glands, development of hair, development of external genital organs. In addition to the morphological modifications of the genital organs the precocious appearance of menstruation is observed.

The syndrome of genital hyperfunction in both sexes is manifested in childhood and assumes the character of pathological manifestation of hyperfunction of the genital glands: Hyperovarianism in women and hyperorchism in men. Among the characteristic symptoms in males there must be cited an abnormal increase in height, the precocious appearance of pubic and axillary hair, and the enlargement of the genital organs; the psychological changes and voice changes; sexual desire appears prematurely. Etiology and pathology show that hypergenitalism or macrogenitosomia represents a disorder of endocrine equilibrium. The literature shows that cases of macrogenitosomia may have a primary character, that is, when there are morphological modifications in the genital glands themselves; the secondary forms of macrogenitosomia are related to affections of the pineal gland and suprarenal cortex.

In the cases of primary ovarian macrogenitosomia the presence of such ovarian tumors as adenocarcinoma, folliculoma and sarcoma is most frequently encountered. In the secondary forms, an important position is occupied by the affections due to pathological states of the pineal gland. Most frequently, such an etiology is related to the destruction of the pineal by tumors (teratomas, gummas, tuberculomas, hydrocephalus). In such cases of destruction of the pineal gland, the latter is unable to restrain the appearance of genital manifestations.

Moreover, as frequent cause of precocious puberty, tumors of the suprarenals must be considered: these tumors are most frequently hypernephromas, from the morphological viewpoint, which implies the increase in function of the cortical substance. The suprarenal cortex, according to its functional role, presents a synergistic action with the genital glands. That is why it is natural that increase in the intensity of the functions of the cortex substance of the suprarenals should produce a stimulating action on the development and growth of the genital organs and also contribute to the development of the secondary signs and growth of hair.

Hypergenitalism is not always a monoglandular endocrinopathy (affection of the ovary, of the pineal or of the suprarenal) and cases have been described in which simultaneous lesions of the ovaries and suprarenals have been observed. In these complex cases of hypergenitalism, symptoms of Addison's disease were present. In the cases where the macrogenitosomia bears the character of polyglandular etiology, obesity may be added to the precocious increase in height and to the development of the secondary sex characteristics.

In certain typical cases, in the presence of a monoglandular endocrinopathy, the diagnosis does not present special difficulties. In other numerous cases, in the presence of a polyglandular etiology, the diagnosis may be difficult. On the one hand, it is difficult to discover the participation of the affected glands and, on the other, it is not always easy to differentiate hypergenitalism from gigantism. The examination of the epiphyseal zones may establish the boundaries of the

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hypergenitalism and the gigantism; at times radiography decides the question one way or the other. In gigantism, the epiphyseal zones remain ununited for a long time; whereas in hypergenitalism, with precocious puberty, the arrest of growth in height takes place towards the age of 8 or 10 years.

In complicated cases, to discover the etiology and differential diagnosis, the reaction of Luttge and Mertz may be used.

Prognosis is intimately related to the etiology and the degree of specific involvement of the endocrine glands. Certain slight cases may be regarded as a manifestation of an almost physiological hyperovarianism following which precocious puberty supervenes and a regular menstrual function. The prognosis becomes more complicated in the cases where following the appearance of precocious menstruation in children, a prolonged loss of blood occurs whose real cause is malignant degeneration of the ovaries: their total ablation does not always suffice to prevent malignant recurrences in other organs.

Where hypergenitalism is intimately related to infectious, syphilitic, tuberculous processes, specific treatment may give a positive symptomatic effect as far as cessation of the menstruation is concerned and regulation of the endocrine equilibrium. At times the regression of all the signs of precocious puberty is observed. Such a result is at times possible in the rare cases where the hypergenitalism has developed following a neoplasm of the genital glands, which has been subjected to radical ablation of the affected glands.

Treatment, according to the case, is directly related to the importance and character of the lesion of one or the other gland dominating this endocrinopathy. In the greatest number of the cases where a malignant affection of the pineal or suprarenals is involved, it is impossible to obtain cure. In certain cases, satisfactory results may be obtained with applicatior of roentgen therapy to the ovarian region.

Organotherapy gives an inconstant symptomatic result, although adrenalin is sometimes capable of arresting the flow of blood in precocious menstruation. Serotherapy by the serum of castrates does not give appreciable result in the cases of considerable hemorrhages. In the symptomatic treatment of hemorrhage due to precocious menstruation, one can at times apply irradiation to the spleen by the x-rays.

Recently the specific action of thallium has been mentioned. Thallium preparations would be capable of inhibiting the production of ovarian hormones and the processes of ovulation. It is also legitimate to employ them in certain forms of hypergenitalism.

The Different Forms of Involution of the Corpus Luteum in Women. — M. Lucien. (*Rev. franç. d'endocrinol.*, 6 : 358, Oct., 1928.)

In the ovary of the human female the regression of the corpus luteum takes place according to two special forms, terminating in the simple fibrous evolutive corpus luteum and the degenerative fibrous corpus luteum or corpus albicans. The involutive fibrous corpus, which may be considered as the normal termination of the lutein involution, results from the banal hyperplasia of the connective elements of the corpus luteum evolving simultaneously with the fatty degeneration of the epithelial cells which atrophy and disappear. This fibrous corpus is but an ephemeral duration and does not take long to amalgamate with and disappear in the ovarian stroma.

The degenerative, fibrous corpus or corpus albicans appears following the brusque involution of the corpus luteum; it is preceded by the necrobiotic degeneration of the epithelial elements and is manifested suddenly by the precipitation of fibrils amid the collagenous protoplasmic ground constituted by the mortified cells. It is the result of a metamorphosing degeneration. The corpus albicans, which has become a foreign body in the stroma of the ovary, remains there permanently. The formation of the corpus albicans may be considered as a pathological phenomenon in relation to the disturbances of ovarian vascularization. Similar processes of involution of the corpus luteum are of a nature to disturb the normal rhythmic functioning of the ovary and to result in quite a series of pathological manifestations in the genital apparatus of women.

Pharmacologic Investigations concerning the Effects of Placenta Extract. — Kosakae. (*Japan J. Obst. and Gynaec.*, **11** : 27, 1928.)

The author carried out experiments with a placenta extract and a preparation prepared from human placenta through hydroly-

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splitting by means of acid. Both extracts had a stimulating effect on the surviving uterus of the rabbit and occasioned rise in tonus and increase of the pendulum rhythm in the surviving intestine. Moreover, through the action of this extract, respiration is increased, the blood pressure in the pregnant animal is raised, otherwise lowered. The author believes that he may conclude from his experiments that placenta extract presents a stimulation to the parasympathetic nervous system.

Thymus Gland. — Nitschke. (*Münch. med. Wochenschr.*, **75** : 1782, 1928.)

The author believes that he has obtained an active thymus extract from the thymus, which calls forth the complete picture of tetany, in animals. In addition a second substance may be obtained which markedly lowers the calcium content of the blood.

Concerning the Substitution Theory in Addison's Disease. — Lange. (*Münch. med. Wochenschr.*, **75** : 1740, 1928.)

Following animal experiments with injection of adrenal cortex extract, the author tried clinically the effect on patients with Addison's disease. In the patients he did not use extracts but the material used for the preparation of the extract, administered orally. The first patient had the complete symptom complex of Addison's disease and so great an adynamia that he could only remain out of bed a short while. In 8 weeks of treatment, in which 5 grams of substitution preparation were given daily, an essential change slowly occurred in the patient's condition. There was a gain in weight of 5 kg.; the adynamia disappeared entirely; the patient took walks of several hours duration without interruption or fatigue. The accumulation of pigment in the skin and mucosae definitely decreased. In a second patient under treatment for the past 3 weeks, a gain in weight of 2 kg. and an indisputable lessening of adynamia were noted.

Hyperthyroidism and Diabetes. Considerations concerning Diagnosis and Treatment. — Carrasco Formiguera. (*Med. Ibera*, **22** : 419, Nov. 3, 1928.)

In the author's personal series, which comprises 1,450 diabetics, there are at least 33 in which the existence of hyperthyroidism was suspected; 23 in which this disturbance was clinically very probable and 20 cases of certain diagnosis. Of these 20 cases there are three in which the nature of the glycosuria may not be diabetic; there remain, therefore, 17 cases of coexistence of hyperthyroidism and diabetes.

The author limits himself to some considerations on diagnosis and treatment. In the presence of a case of hyperthyroidism, diabetes must be thought of and an investigation made for glycosuria and induced hyperglycemia, in order to rule out non-diabetic glycosurias. If the curve of hyperglycemia is of diabetic type, it is a case of true diabetes.

The author has the impression that it is of frequent occurrence to fail to diagnose hyperthyroidism in patients qualified as diabetic. He refers to those cases of hyperthyroidism which do not present exophthalmos, or do not present visible goiter, but nevertheless a slight enlargement in size of the thyroid. In these cases in which nothing attracts the attention of the clinician, it is necessary to be guided by the sensation of asthenia and by the loss of weight which can not be explained by the diabetes, since digestive disorders, irritability, exaggerated emotivity, a tremor and tachycardia are frequently attributed to the diabetic condition.

The ideal procedure would be for the physician to systematically determine the basal metabolism in diabetics; but as this is possible only in the great centers of clinical investigation, the physician must search for some of the above mentioned symptoms of hyperthyroidism and in case he finds them, make a determination of the basal metabolism, the sole method of establishing the diagnosis with certainty.

One of the findings which has most frequently suggested hyperthyroidism to the author has been the persistence of loss of weight and strength or the failure to gain even after treatment of the diabetes has brought about a disappearance of the glycosuria with a sufficient diet to obtain a good state of nutrition.

In order that the basal metabolism test may have its full value, it is necessary that this test be carried on when the patient is not glycosuric and has been submitted to a diet that is not loaded with proteins and sufficient to cover the nutritive needs (which can be foreseen independently of the hyperthyroidism). Insulin has made it possible to completely eliminate the unfavorable influence

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of diabetes on hyperthyroidism; so that the prognosis will depend solely on the degree of thyroid disturbance.

Treatment consists in (1) eliminating or reducing to a minimum the factors which in addition to hyperthyroidism may be the cause of the raised metabolism. For which reason it is necessary to avoid the action of cold, to limit as much as possible muscular exercise and reduce the protein diet to the lowest limit compatible with the balanced nitrogen intake; (2) administering sufficient food to cover the energy requirements of the organism, abnormally raised by the hyperthyroidism; (3) increasing as much as possible the metabolic capacity of the organism, for which the necessary quantity of insulin is administered for the necessary amounts of glucose to be tolerated.

In the great majority of cases the adoption of these methods has as effect the rapid and more or less considerable improvement of the general condition, increase in weight, in strength, or at least maintenance of weight, decrease of tachycardia, and nervousness. At times this improvement of the general condition becomes very important.

As the plan of treatment described does not influence the hyperthyroidism at all, the result is that any increase in muscular activity or any decrease in the supernormal amount of food causes loss of weight and of strength and change for the worse in the general condition. In no case did insulin cause any improvement in the thyroid disturbance. For this reason, thyroidectomy, irradiation or anti-thyroid organotherapy will be necessary, according to the case. The author believes that in the majority of cases the better transition for the latter treatments is to be obtained by the administration of small doses of iodin.

Liver Extract and Tropical Anemia. — A. Díaz Albertini and J. Rodríguez Pérez. (*Vida Nueva*, **22** : 191, Sept. 15, 1928.)

The authors report the results they have obtained in many cases of tropical anemia by treatment with liver extract, four cases being reported in detail. The study of these cases again shows the remarkable action of liver in these anemias. Under the influence of liver the number of red blood cells increased considerably and at the same time the proportion of hemoglobin increased. In consequence, the general state of the patients improved notably, the diarrhea disappeared from the very beginning of the treatment and the tongue soon resumed its normal aspect. The authors kept control of the blood sugar of the patients, because experience has shown that by maintaining it at figures around 90 mg. per 100 cc. of blood, the most favorable results are obtained, and because in this way the appetite is stimulated and the protein diet may be amplified by the addition of carbohydrates (but not by fats which are poorly tolerated). In general, five units daily of insulin sufficed.

The authors call attention to the low monocyte count in advanced cases. These increase in number as the improvement becomes more marked and remain in relatively high figures among the normal.

On the other hand, the lymphocytes in general decrease in number, coinciding with the improvement noted in the processes, and in consequence, they have great importance from the viewpoint of prognosis.

The authors have not yet had sufficient experience with the therapy to speak of the future of these individuals. They can not tell whether the patients will have to continue taking liver extract indefinitely or whether the results obtained will be maintained causing the reactivation or a permanent improvement in the functions of the liver and perhaps an anatomic regeneration equivalent to a cure. At the present time, the authors believe that permanent improvement may be obtained in young individuals. This is not the case in older patients whose completely exhausted liver must be substituted for, and logically the liver treatment will have to be continued indefinitely in these cases.

In concluding, the authors state that a liver preparation with these properties constitutes a considerable advance in modern therapy. Next to insulin, it is the most beneficial force which has been realized in the field of medicine.

With liver extracts the authors have been able to obtain brilliant results in cases where a short time ago there would have been no successful therapeutic agent.

Movement of Water in the Organism. — Mautner. (*Deut. med. Wochenschr.*, **54**: 1824, 1928.)

The movement of water in the organism is dependent upon physico-chemical reactions, muscle contractions, etc. In the gastro-intestinal canal in which not only absorption

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but still more secretion of water takes place, it is the contractions of the intestinal villi which essentially influence the processes of water movement. Yeast extracts, for example, stimulate here. On the other hand, secretion and peristalsis influence the absorption. Nervous stimuli and hormones, for example, the absorption-favoring insulin by way of the hypoglycemic attack and pituitrin, further or restrain absorption. Concerning the complicated processes in the passage of water over into the blood, little is known. The mechanical pressure in the capillaries is decisive for the mechanism of the extravasation of water into the tissues. The essential regulation site lies in the liver, in which the contraction of the liver veins inhibits or enhances. In contraction of the liver veins there may result extravasation of water from the capillaries to the veins, so that following a drink of water a dripping on to the liver surface can be observed. Here also not purely mechanical but also hormonal influences are at work. In the kidneys too not only filtration or expressing but also vital processes and nervous influences are active. In perspiration an inactive phase likewise must be assumed through which the water can enter through skin or lungs. The water deposits are also involved in the regulation of the water stability, the activity of which is restrained through a regulating center. A diuresis inhibition proceeds from the cerebrum; the diuresis center lies in the vicinity of the tuber cinereum, of which one part is connected with the pituitary. Pituitrin, which streams directly into the third ventricle, acts as a stimulus for the part of the diuresis center situated here. The adequate stimulus for this center is probably the oncotic pressure of the circulating albumin and the changes of the blood albumin picture. In addition, nervous influences, salt content and reaction of the blood and above all glands with internal secretion play a rôle.

Clinical Value of the Ovarian Preparation Prepared According to the Method of Stern-Batelli. — A. Kogan and L. Libin. (*Arch. Gynäkol.*, **135** : 262, 1928.)

The frequent lack of result in the use of ovarian preparations encountered commercially may be explained by the fact that the ovaries like other endocrine glands, possess no store of specific hormones, but secrete them in the quantity in which they arise in the blood. An active preparation could therefore only be prepared when the gland concerned continues to live following its removal from the organism and can secrete its secretion products into the environs. The method of Stern-Batelli rests on this principle: the ovaries were cut into fine pieces, placed in Ringer's solution previously warmed to 38° and saturated with oxygen; 10 cc. of Ringer's solution to every 1 gm. of tissue. The tissue remains 20 to 30 minutes suspended under a supply of oxygen at body temperature; the fluid is frequently changed. Finally, the whole fluid is filtered and used without further treatment. For the most part, 50 to 100 cc. were administered once or twice daily per rectum. The preparation was given in 62 cases. In 12 women of 22 to 43 years, in whom the uterus and ovaries had been removed, and severe deficiency symptoms existed, increase of deficiency symptoms appeared during the first weeks of treatment, followed, however, by essential improvement. These women had previously been treated with organ preparations altogether without result. The same thing occurred with 8 patients in the climacteric with symptoms of ovarian insufficiency, in whom improvement was obtained through the preparation. Moreover, 22 women with amenorrhea (in part with underdevelopment of the genitals) were treated with this preparation. These women had also been treated previously without result with organotherapy. With the Stern-Batelli preparation regular menstruation was obtained in one part of these amenorrheic cases. Finally 16 patients from the Neurological Clinic (12 basedowoid and 2 with pronounced exophthalmic goiter) were successfully treated with this preparation. In order to effect complete stimulation of the ovaries a 4 to 6 weeks treatment is necessary.

Modern Treatment of Diabetes in Children.—R. Wagner. (*Wien. med. Wochenschr.*, **78** : 1139, 1928.)

If the diagnosis of diabetes has been made in a child, then insulin should be given at the outset even if sugar can be removed without insulin. For in the first place it is easier with this therapy to get rid of an infection to which the children are frequently exposed and secondly, with simultaneous treatment with insulin, more carbohydrate may be given to the child, which is of great

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importance in childhood. If a child is received in coma, 50 to 60 units are given intravenously as initial dose and the injections are repeated in small doses every 2 to 3 hours within the first 12 hours. When vomiting has ceased and respiration has improved, the doses of insulin must be lessened in order not to induce hyperinsulinism. Small children are very sensitive to insulin and easily become hypoglycemic. In this case, when an oral administration of sugar is not possible, 10 per cent glucose solution is given subcutaneously.

Acrocyanosis of Young Women. The Physiopathologic and Pathogenic Importance of Venous Hypertension and Ovarian Insufficiency. — M. Villaret and F. Saint Girons. (*Arch. Méd. Enf.*, **32** : 79, Feb., 1929.)

The authors have observed the existence of a syndrome characterized by three factors in a rather large number of patients ranging from 15 to 20 years: acrocyanosis, ovarian insufficiency and increase of venous tension. The young women have had irregular menstrual periods from the beginning of menstruation; obesity is at times important and is generally distinct. All present a very marked cyanosis of the hands, less marked of the feet, with edema and chilling; the disturbances are very marked during the winter where they terminate in painful frostbites; these frequently ulcerate and resist the classic treatment as long as the weather remains cold. Otherwise, the patients give no clinical sign of disorder or anomaly of the circulatory, respiratory, urinary or nervous system. However, in contrast to a maximum normal arterial pressure, their venous pressure is constantly increased.

It seemed to the authors that this syndrome was intimately related to the existence of ovarian disorders as shown by the irregularity of menstruation and the frequent obesity. It is a question of endocrine cyanosis, for ovarian organotherapy has given definite results, especially in one case (improvement of the subjective disturbances with improvement in the menstrual periods, indisputable decrease of cyanosis and slight fall of venous pressure).

The authors do not wish to give the impression that all cases of acrocyanosis are of ovarian origin but merely wish to show that some cases of this disturbance have this etiology. It appears also that the ovarian disorders which are the cause of the cyanosis and venous hypertension are solely disturbances of hypofunction. In fact one woman whom the authors had occasion to observe was suffering from obesity of thyro-ovarian origin with vertigo, headaches, sweating, increase of menstrual flow, and presented severe metrorrhagia whenever ovarian therapy was attempted. In this case of hyperovarianism the venous tension was not only not increased, but was distinctly below the maximum arterial tension.

The interest of the syndrome resides especially in its pathogenesis. Venous hypertension need not be dependent upon a cardiovascular affection alone but may also result from an endocrine alteration. It is also worthy of notice that the venous hypertension and acrocyanosis may decrease in parallel manner under the action of ovarian therapy.

Spleen and Rickets. — R. Soula and Cauquil. (*Paris méd.*, **18** : XIII, 1928.)

Rickets can only be an endocrine insufficiency of elaboration of sterins. This elaboration which under normal conditions probably takes place through the spleen and reticuloendothelial system, is insufficient in rickets. It can be corrected through irradiation and organotherapy.

Pituitary Dwarfism. — Dr. and Mme. Schiff. (*Paris méd.*, **19** : xxx, Jan. 5, 1929.)

The authors present a patient of 14½ years whose physical growth has been completely arrested since the age of nine years. At that time a syndrome of cranial hypertension expressed itself in intense headaches and vomiting. Two years later, the child became suddenly and totally blind. The headaches have persisted since that time. At the present time there exists a complete atrophy of the optic nerves, a slight hydrocephalus, a considerable enlargement of the sella turcica upon radiography. Outside of the dwarfism a fall of basal metabolism of 26 per cent and a testicular sclerosis were noted. The Bordet-Wassermann test of the blood was negative in the subject and his mother. Specific treatment prolonged for 4 years, remained ineffective.

The authors discuss the indication for a surgical intervention (transphenoidal ablation, transfrontal puncture), despite the irremediable loss of the vision, and the

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utility of the radiotherapy, which would have to be very prudent because of the great radiosensibility of the nervous cells of the child.

Painful Vasomotor Disorders in a Case of Dysendocrinism. — M. Scharrenberger. (*Presse méd.*, **37** : 146, Jan. 30, 1929.)

The patient, a young man of 20 years, presented painful pricking of the hands and feet; at times, paroxysmal pain accompanied by pallor and coldness of the fingers and toes; at times cramps. Beginning at the age of 10, the present condition has existed since the age of 14 years. The disturbances came on without apparent cause. The subject was never able to do any appreciable work.

On examination there was noted a feminine habitus, a dysthyroidism and signs of sympathetic disequilibrium. The patient's hands were smooth, pale in color, warm to the touch, of weak muscular strength in proportion to the slenderness of his extremities, without pyramidal deficiency. Normal objective sensibility; no pain on pressure. In short, an association of endocrine sympathetic signs in a young man presenting painful vasomotor symptoms.

Concerning Hyperglycemia in Acute Disease of the Pancreas. — F. Bernhard. (*Deut. Zeitschr. Chir.*, **212** : 217, 1928.)

Hyperglycemia is an important symptom of acute disease of the pancreas. The cause of hyperglycemia is to be attributed to lack of insulin. For this reason, energetic insulin therapy is recommended in acute necrosis of the pancreas.

Investigations concerning the Influence of the Thymus on Muscular Activity. — O. Held. (*Zeitschr. Biol.*, **88** : 76, 1928.)

The author performed experiments with thymus extracts which were injected part subcutaneously, part intravenously and tested the influence of thymus preparations on the phenomenon designated as "apparent fatigue." This apparent fatigue is removed, as this experiment shows, by subcutaneous and intramuscular injection of thymus preparations. It is not the effect of an albumin substance. The action of thymus preparations is shown on the working muscle itself, whose ability for work is heightened. Control experiments with Ringer's solution were negative. Intravenous injection of adrenalin solution did not have the same effect as thymus preparations.

Studies of Calcium Metabolism in Certain Diseases of the Skin. — N. Burges. (*Brit. J. Dermat. and Syph.*, **40** : 279, 1928.)

Certain dermatoses are dependent on increased irritability of the nerve cells, caused by lack of calcium in the tissues. The results of treatment show that administration of calcium and thyroid preparations in dermatoses of nervous origin is of special value. Cases of urticaria, prurigo, eczema and those cases of cyanosis of the extremities and chilblains with low calcium content of the serum were considerably improved with calcium and thyroid therapy.

Hormonal Influencing of Sex in Animal Experiment. — Beyer. (*Med. Welt*, **2** : 1528, 1928.)

Resuming the experiments of E. Vogt, Beyer remarks that to the two possibilities of influencing sex — through undernutrition and overnutrition — the hormonal influence may be added as a new possibility. Through this the general law is supplemented, according to which in times of need, under abnormal living conditions more female young are born than male. In this way the preservation of the species is most certainly guaranteed. From this viewpoint the hyperfeminization of the new generation seems to be a sequel to the injuries undergone during the war.

Influence of the Glands with Internal Secretion in the Metabolism of the Bones. — Biedl. (*Med. Welt*, **2** : 1544, 1928.)

In embryonal life and shortly after, the interrenal system (adrenal cortex) and the sex glands are especially influential, on the contrary, the thyroid minimal. In the phase of puberty, the time especially of growth in length, thyroid activity appears in the foreground, and raises the metabolism. Here we also have hyperthyroid disturbances, the goiter of puberty. The proper growth glands are the thyroid and the pituitary anterior lobe. However, without the growth symphyses remaining open, growth is not possible and the symphyses remain open only so long as the development of the sex glands is not yet complete. Administration of thyroid

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substance can occasion changes in growth and proportions even in adults. The hyperthyrosis causes an excessive growth in length in the growing individual. Pituitary dwarfism can be improved by administration of pituitary substance. The pituitary anterior lobe is a growth gland. Premature development of the sex glands can also be influenced by feeding of pituitary.

Neuroses Conditioned by the Endocrine Glands. — F. Boenheim. (*Arch. Verdauungskrankh.*, **42** : 383, 1928.)

The author contributes histories of patients and disease pictures in order to draw the attention of physicians to the etiological significance of endocrine disturbances for neuroses, psychoses and hysterias. The recognition succeeds only through exact somatic investigation with respect to the endocrine function. The thyroid probably produces a whole series of different hormones so that in dysfunction of the thyroid the most diversified disease pictures can arise. Boenheim sees a corroboration of his conception of the endocrine genesis of many neuroses in the therapeutic activity of specific organotherapy, for example, whole pituitary suppositories.

A Case of "Ovarian Diabetes," Resistant to Insulin, Very Much Improved by Folliculin. — Carnot, Terris and Caroli. (*Bull. et mém. soc. hôp. Paris*, **44** : 738, 1928.)

A 36 year old patient, in whom diabetic symptoms and amenorrhea arose simultaneously. Daily excretion of sugar up to 100 gm., at times acetone, marked emaciation, distinct variations with the menstrual cycle. Neither dietetic nor insulin therapy had any effect. Following injections of folliculin, decrease of urine and blood sugar. Gain in weight.

Rise in Blood Pressure and Extirpation of the Spleen. — Hercher. (*Zentr. Chir.*, **55** : 2350, 1928.)

The author refers to the repeatedly observed threatening fall of blood pressure, which appeared following the use of spleen extract. The question whether it is a matter here of a hormone action or an anaphylactic manifestation is not yet clear. Can the rise in blood pressure following extirpation of the spleen be considered as an effect of removal of the organ, perhaps conditioned by a loss of an internal secretory principle of the spleen?

Internal Medicine and Chemistry. H. Horsters. (*Med. Klin.*, **24** : 1441, 1928.)

A new branch of chemical therapy has arisen with the discovery of adrenalin: hormone therapy which can also be designated as constitutional therapy. Here medical chemistry in clinic and laboratory has celebrated triumphs with the discovery of insulin. In synthetic thyroxin a further important step in this field has been made. Liver therapy in pernicious anemia promises new discoveries in the ranks of substitution therapy. The important task is here reserved for the chemist to isolate the sum of the active principles and present it pure. The closest joint work with the clinic is indispensable for the experiment. In respect to the purification of organ extracts, however, nature orders a halt, according to all appearances, in that it has been shown that in a part of these substances a too extensive purification in the sense of the isolation of a chemically defined substance often leads to decrease of activity. In this connection the work on insulin must be remembered.

Diuretics. — A. Herz. (*Wien. klin. Wochenschr.*, **41** : 1378, 1928.)

Thyroid preparations act extrarenally in dropsy with lowered thyroid activity and in nephroses. Their use is contraindicated in cardiac edema, in nephrosclerosis, hematuria and hyperthyroidism. Control of the pulse and of the properties of the urine is absolutely necessary in thyroid medication. Thyroid tablets should be given in a dosage of 0.3 gm. at the beginning increasing to 2 gm. after about 2 weeks.

Practical Therapeutics

(*Continued from page 145*)

anism of action as the continuous absorption of minute amounts of nitrite ions, thus causing gradual relaxation and rest. He summarizes as follows:

"1. Variations in the chlorid content of the blood do not affect the arterial tension to any major degree.

"2. Administration of bismuth subnitrate causes a slight reduction in the chlorid content of the blood, as do other nitrates, through the production of a chlorid diuresis.

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"3. Administration of bismuth subnitrate assists materially in obtaining a reduction in arterial tension in hypertension, both in non-pregnant and pregnant cases.

"4. The therapeutic results are much better when arteriosclerosis is not marked.

"5. A method of evaluating therapeutic results in hypertension in terms of percentage return to normal is presented.

"6. The pharmacodynamic mechanism of bismuth subnitrate in hypertension is a dual one:

"*a.* Gradual vasodilation by continuous absorption of small quantities of nitrite (NO_2^-) ions.

"*b.* Reduction of the blood chlorid content by diuresis initiated by the nitrate (NO_3^-) ions.

"7. The fundamental value of bismuth subnitrate in hypertension lies in its property of breaking the vicious circle of vascular fatigue, hyperirritability, with more spasticity and fatigue and thereby permitting of physiologic *rest*."

Hypertension is of unknown etiology as far as the ultimate causes go. The treatment, therefore, is partly symptomatic and expectant. Perhaps no condition claiming the attention of a physician requires so much individual study. The careful physician, however, can accomplish much in most of his cases.

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A Case of Intersexuality of Hermaphroditic Type. — G. Marañón. (*Med. Ibera*, 22 : 381, Oct. 27, 1928.)

The states of intersexuality in the clinic may be divided into the following groups: hermaphroditism, masculine or feminine pseudo-hermaphroditism, virilism and feminism, cryptorchidism and hypospadias, gynecomastia, homosexuality and other functional intersexualities, intersexualities of puberty and the climacteric, partial intersexuality in normal subjects. Of all these types of intersexuality, the most unusual is hermaphroditism. Nevertheless, it is probable that the true hermaphroditism, that is, the simultaneous presence of two sex glands in the same individual with the corresponding coexistence of the characters of both sexes, is much more frequent than supposed. In fact, in order to be certain of the existence of the mixed sex glands or ovary-testis, it is necessary not to limit oneself, as is generally done, to the examination of a single genital gland extracted during a surgical intervention, but the two glands must be studied carefully, since in the majority of cases the ovary-testis is limited to a single side and perhaps to one of the poles of the sex glands. For this reason, various cases diagnosed as pseudo-hermaphroditism, that is, of inverted appearance with normal sex glands, must be in reality true hermaphroditism incompletely studied. To this group belonged without doubt an intersexual who was exhibited at fairs in Spain and who was recently studied in the author's clinic. He is sixty years old and reports that he has menstruated up to about fifty years. His appearance is mixed. The distribution of fat, the comparative proportions of his pelvis, and scapular girdle, the pubic hair and above all the breasts are those of a woman. The hair and voice are masculine. He states that his instincts are also virile and that he has had frequent sexual relations with women. The genital organs show a penis the size of that of a boy of about 15 years, without urethra. This opens one centimeter below, and 2 cm. lower a small vaginal conduit opens. The labia majora have the appearance of empty scrotal sacks.

This case would usually be diagnosed as one of feminine pseudo-hermaphroditism; Pozzi labeled it such 26 years ago. The equal presence of both sexes, however, suggests a case of true hermaphroditism. In this case, however, as in others, an exact diagnosis could only be made after histological examination of the sex glands.

General Therapy of Skin Diseases. — Otto Kren. (*Wien. klin. Wochenschr.*, 41 : 1404, 1928.)

Organotherapy attempts to improve the function of diseased organs, or to replace

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their chemical function. As is well known, the endocrine glands also secrete substances peculiar to them, of which each one has a very special task to fill for itself in the body. These substances are the hormones. To carry out a correct hormone therapy, signifies being acquainted with the action and symptoms of abolition of function of the endocrine glands with their effects on the skin and the organism in general and treating them accordingly. In this respect it is to be mentioned that frequently not only one gland is disturbed in its function but the whole harmonious interrelationship of all glands, that, therefore, obviously several glands are functioning abnormally and for this reason call forth a disturbance.

Pulvermacher recently reported investigations, therapeutic results and experiments and arrived at results full of contradiction. One is, however, certain: Each of the endocrine glands can produce substances in disturbed function which sensitize the integument and so give occasion for the origin of a dermatosis. Whether the secretion itself forms a hormone, as is claimed by some authors, which is also involved in the course of the dermatosis, must be determined by further investigation. The type of treatment consists for the most part in the administration of the missing hormones or in roentgen stimulation of the organs concerned. In the administration of the hormone the subcutaneous or intravenous form of administration is in each case superior to the oral.

Animal Experimental Investigations concerning the Pituitary Anterior Lobe Hormone with Special Reference to the Reproductive Phases. — Schultze-Rhonhof. *Deut. med. Wochenschr.*, **54** : 1702, 1928.)

Typical changes are found in the vaginal mucosa even in castrated animals 72 hours following injection of ovarian preparations. Pituitary anterior lobe implant in still immature mice results in sexual precocity in 80 to 100 hours and simultaneously to change of the vaginal mucosa. In castrated animals, pituitary anterior lobe has no influence. In an infantile mouse even the implantation of the pituitary of an 80 year old individual had a marked influence. Infantile hypophyses implanted into infantile animals likewise result in signs of pronounced ovarian function, even when the implant came from animal fetuses; human fetal organs acted only to 50 per cent. Through simultaneous implantation of anter... pituitary and thymus, the origin of est... was for the most part prevented.

Relations between the Digestive Tra... and Blood Diseases. — Schottmüller. (*Me... Welt*, **2** : 1538, 1928.)

Liver powder gives the best results. I... "liver remissions" increase in reticulocyt... occurs after 1 week; after 8-14 days increas... in erythrocytes and hemoglobin occur. Th... manner of action of liver is still unknown— hormonal or detoxicating? Analogous to live... therapy in pernicious anemia, spleen trea... ment is to be tried in hyperglobulia.

Arthur Hartmann

(*Continued from page 147*)

and relating to physicians. He attended meetings of many medical societies at which he sometimes contributed and sometimes presided; he abstracted material for these meetings as well as for several publications in which he took an interest. The journey to England and France was a kind of self-imposed apprenticeship through which he was able to bring to his own country the best knowledge and experiences of the workers in other countries. He served on Medical Boards in both active and advisory capacities. The desire to reform and improve medical study prompted Hartmann to make a survey of courses of instruction for physicians especially in England and France and also in other countries of Europe. He presented his findings in several essays and drew up a new system for Germany. As a member of the *Schuldeputation* in Berlin and as an official in charge of City Hygiene, Hartmann instituted a course of special training for school doctors, for it was his belief that physicians must be especially trained to handle children. He assisted in establishing a school for the instruction of deaf and dumb individuals based on the principles derived from his researches in this special field.

As evidence of a practical bent, there are several instruments invented by Hartmann for use in the treatment of diseases of the ear, nose and throat. They are still in use under his name.

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The Theory of Insulin Action. — Schur. (*Klin. Wochenschr.*, 7 : 1983, 1928.)

Schur is of the opinion that insulin attacks the assimilation process in such a way that it effects the deposition of carbohydrate in the fat tissue and its transformation into fat tissue. Proceeding from this standpoint, the author undertook determinations of the total carbohydrate in the fat tissue with a new method, according to Dische and Popper, and constantly found quite considerable amounts of carbohydrate as well as a quantitative influencing of it through administration of carbohydrate. Insulin probably also has a direct effect on the deposition of lipoids. It appears, therefore, quite generally to have a furthering influence on the deposition of food substance ingested.

Porges, Vienna, proceeding from the viewpoint that even in normal individuals a diet rich in carbohydrate raises the carbohydrate tolerance, gave diabetics a diet rich in carbohydrate (with the use of large doses of insulin), thereby a diet rich in albumin but poor in fat with a considerable increase in tolerance as a result.

Discussion: Adlersberg is of the opinion, according to his experiments, that the retrogression of the urinary sugar in this form of diet is dependent upon an increased density of the kidneys. Minkowski, Wiesbaden, doubts this and considers the rise in tolerance obtained to be dependent upon the large amount of insulin used. Porges stresses that the rise in tolerance is also obtained without insulin and even with the use of insulin appears only when abundant carbohydrate and little fat are given, not, however, when little carbohydrate and a large amount of fat are given.

Nature and Treatment of Hyperemesis Gravidarum. — Runge. (*Zentr. Gynäkol.*, 52 : 2547, 1928.)

Insulin is no longer to be dispensed with in the treatment of hyperemesis. It is, of course, understood that care must be taken that carbohydrate be administered before the injections, either in the form of sugar water or, when that is not tolerated, in the form of rectal injections. To overcome the severe conditions of emaciation in this disease, insulin forced feeding offers quite an essential support in doses of about 5 units. The appetite increases, there is gain in weight. There is no question but that insulin is an extraordinary adjuvant to therapy in this condition. Runge is altogether of the opinion of Heynemann with respect to the specific action of insulin. It is as little a question of a specific effect in the insulin effect here as in any other remedy used up to the present in hyperemesis.

Action of Thyroxin on the Heart. — M. Nothmann and G. W. Parade. (*Klin. Wochenschr.*, 8 : 699, 1929.)

The sharply defined relationship between hyperthyroidism and cardiac symptoms, as well as the great rôle claimed by thyroid gland therapy due to artificial incorporation of thyroid gland incretion by the method of Kendall and Harrington, gave the authors the impetus to investigate the action on the heart of doses of thyroxin administered intravenously and perorally. They used for the experiments synthetic thyroxin derived according to Schering and employed the method of Schoeller. In the metabolism experiments conducted by Lublin, it was seen that this preparation acted to increase the basal metabolism.

The effect of thyroxin was observed on the healthy heart and on a series of cardiac patients. Report will be made later concerning their tests on thyroid gland patients.

In twenty patients, neither after intravenous (two doses, 5 mg. per dose) nor in *per os* administration (three times daily, 1 mg., 2-4 weeks duration) did they see any signs of hyperthyroidism whatever. The general condition was in no way disturbed.

The pulse frequency in persons with healthy heart showed, similar to the investigations of Baur and Loewe, no increase, if we accept as a psychic factor the rare occurrence of 10 beats increase per minute immediately after injection. Likewise irregularities of pulse were never induced. In three cases of absolute arrhythmia, a striking increase in frequency was observed after injection of small doses, which was less conspicuous after large doses. With intravenous injection of large doses the author was under the impression, often, that the pulse was noticeably slower.

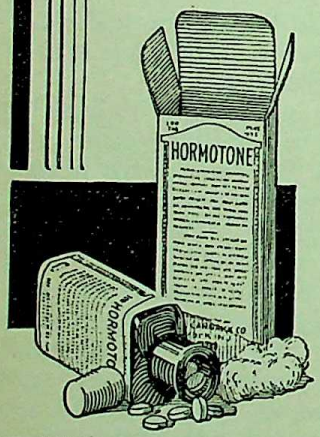
The most important of the authors' investigations are concerned with the effect of thyroxin on the course of the electrocardiographic curve. In their normal cases neither was there any effect to stimulate the heart itself nor any other part of the body. The configuration of the auricle or ventricle complex was never altered. In cases of auricular

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flutter or auricular fibrillation with absolute arrhythmia of the ventricle the authors observed no increase in the fibrillation symptoms of the cord. After small intravenous doses of thyroxin, the often improved, increased discharge of the ventricle, running parallel with a striking increase in pulse frequency, was seen which can be spoken of as a cursory improvement of transfusion. In one case of entire dissociation based on luetic cardiac affection, neither was the sinus frequency increased nor were the secondary centers of the ventricle affected.

In conclusion, the authors state that thyroxin, of the forms of medication chosen by them, does not act on the pulse frequency or the course of the electrocardiographic curves.

Castration in Pregnancy. — Waldstein. (*Wien. klin. Wochenschr.*, **42** : 380, 1929.)

Both ovaries were removed from a woman with bilateral dermoid cysts in the second month of pregnancy, a normal termination of birth resulted in a child weighing 3500 gm. taken by forceps. The case was subjected to quite elaborate hormone study. The ovarian hormone content of the blood serum was quite like that of normal women. In desiccated extract of the placenta about 300 mouse units of ovarian hormone were determined, a rather insignificant amount, but as the investigations on the subject show, it can be indicated as normal, since even in normal placentas a similar amount can be found. From the above experiments the following conclusions were obtained:

1. Ovarian hormone does not originate in the ovary, but rather in the placenta.
2. The placenta does not store the hormone.
3. The hormone produced from the placenta was given into the blood *in statu nascendi*, for as much ovarian hormone could be found in the blood of the placenta as occurs in the whole placenta. By means of these investigations the theory of Halban appeared to be confirmed, whereby the placenta produces "active substances." This is none other than hormone.

The hormone of the anterior lobe of the pituitary was likewise evident after castration, as well as in other pregnant women, so that one can assume that production of the hormone of the anterior lobe of the pituitary was not affected by castration. From the urine of castrated women much less ovarian hormone was isolated than from that of normal pregnant women. The author believes in treating the castration symptoms after the termination of lactation with the hormone derived from the woman herself.

Four weeks after the castration operation the woman suffered a psychosis, for which she was promptly hurried off to a psychiatric clinic.

Sex Hormone in the Urine of Pregnant Women. — Leiv Kreyberg. (*Norsk Magasin for Laegevidenskapen*, **90** : 379, 1929.)

Ovarian hormone as well as pituitary hormone can appear in the urine. Ovarian hormone is found in the urine in a whole series of body conditions: in pregnancy, at the beginning of the climacterium as well as in certain forms of amenorrhea. In contrast to this, the pituitary hormone appears spasmodically, as it were, in the urine of initial pregnancy and can therefore serve as an efficient indication of early pregnancy. The author adds observations from which the changes in infantile sex organs of the mouse due to pituitary hormone from the urine of pregnant women are indisputable.

Concerning Specific-Dynamic Activity and Pituitary (Rat Experiments). — R. Nothhaas. (*Pflügers Arch. ges. Physiol.*, **221** : 763, 1929.)

By feeding substance from the cortex of the anterior lobe of the pituitary, a specific-dynamic activity occurred in rats in 14 days to 3 weeks (normal about 20 per cent) to a maximum of about 26 per cent increase. Therewith the basal metabolism fell.

Therefore the rat is a suitable test object with regard to the component of the anterior lobe of the pituitary, which initiates metabolism.

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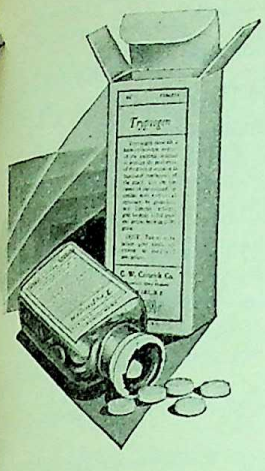
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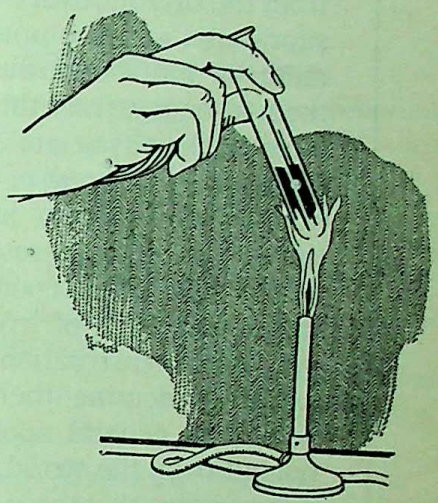
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Insulin, Epinephrin and Sugar Metabolism

INSULIN and epinephrin are important factors in carbohydrate metabolism. Their action is opposed and is exerted in the peripheral tissues. Epinephrin increases deposition of liver glycogen, insulin decreases it.

In considering the sugar metabolism of the body, the oxidations which give rise to the energy supply and the manner in which the nutritive material is stored and released for oxidation, the logical starting point is glycogen. Glycogen is a polysaccharid — a storage sugar — and is found in almost all the tissues of the body, but particularly in the liver and muscles. Glycogen is one of the products synthesized in the body, principally from the carbohydrates but also from the proteins and the products of protein cleavage — the amino acids (1). Whether fat may be converted into glycogen is still debatable.

Under ordinary physiological conditions carbohydrate metabolism is characterized by continuous activity in both muscles and liver. As soon as the dextrose of the blood reaches a low level due to oxidation by the cells the deficit is made good by the glycogen of the liver, which, under the influence of the enzymes of the hepatic cells, undergoes transformation into blood sugar (dextrose). The glycogen of the muscles is converted into liver glycogen by a process which has received considerable attention recently and which is now fairly well understood.

Since it was clearly evident that injection of epinephrin gave rise to hyperglycemia and

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glycosuria, and since the greatest sugar values were obtained in animals rich in liver glycogen, it was assumed by early workers in the field that epinephrin reduces the glycogen store of the liver. Evidence began to accumulate, however, that epinephrin may actually cause a formation of glycogen which is deposited in the liver. Pollak (2) found that in starved animals as much glycogen may be formed by injecting epinephrin as by carbohydrate feeding. Kuriyama (3) also reported increase of liver glycogen following epinephrin injection.

J. Markowitz (4) found that "The injection of epinephrin into starved rabbits always evokes extensive hyperglycemia, even when the injections are kept up for days.

"When the liver is glycogen-free, injection of epinephrin does not lead to hyperglycemia. When the liver contains traces of glycogen, hyperglycemia of delayed onset ensues, the extent being proportional to the amount of glycogen.

"Mere starvation does not make rabbits glycogen-free. Starvation in the cold, followed by strychnine convulsions will make the liver, heart and muscles glycogen-free for several hours.

"Repeated injection of epinephrin into starved, strychnine-treated rabbits permits glycogen to accumulate in the liver, heart and muscles.

"When insulin is given to starved strychnine-treated rabbits along with epinephrin, considerable quantities of glycogen, up to 2.77 per cent accumulate in the liver.

"The above experiments together with those quoted from the literature, demonstrate that glycogen is obligatory, and not an optional step in the formation of blood sugar from the non-carbohydrate stores of the organism."

C. F. and G. T. Cori (5) investigated the whole problem of glycogen formation and the effect of both epinephrin and insulin on glycogen and blood sugar. The earlier views of the action of epinephrin assumed a direct action on the glycogen of the liver. Actu... little investigation appears to have been m... on this point. Since the source of bl... sugar was known to be the glycogen of the li... it was assumed rather than observed that ... increase of blood sugar and glycosuria ... lowing epinephrin injection was due to an a... tion in converting liver glycogen into dextr...

In Coris' work the assumption was m... of an extra-hepatic point of action. Insu... and epinephrin exert opposed actions ... blood sugar. Insulin acts by causing ... mobilization of liver glycogen and there ... no differences in rate of disappearance ... liver glycogen in normal and adrenalectomize... animals following insulin injection. Actua... the site of epinephrin action was found to ... on the glycogen of the muscles rather th... that of the liver. The earlier observatio... of an increase instead of a decrease of liv... glycogen were confirmed. Epinephrin co... verts muscle glycogen first into lactic ac... which is then converted into liver glycog... which therefore increases in amount.

In order to ascertain whether liver glycoge... can be formed from lactic acid, δ-lactic aci... its sodium salt and γ-sodium lactate was fe... to fasting rabbits with a resulting deposit ... glycogen in the liver. This was consonan... also with previous work which showed ... marked increase of lactic acid in the blood ... following epinephrin injections. The po... sibility that epinephrin causes an increase o... liver glycogen by conversion of protein ... glycogen is dismissed as having less evidenc... to support it. In the discussion of one o... their papers the Coris say:

"According to the generally accepted exp... nation epinephrine causes hyperglycemia, an... after large doses, glycosuria, merely becaus... it mobilizes liver glycogen. As pointed ou... in the introduction, hyperglycemia and gl... cosuria can not be explained on this basis ... because there is not enough liver glycogen ... present to provide the tissues for hours wit... sugar at a rate which is greater than th... normal ability to utilize sugar. This is ill...

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rated by the following calculation. In the experiments in Table IV the average blood sugar was 174 mg. per cent 3 hours after the epinephrine injection. In order to produce a hyperglycemia of this magnitude in normal rats, glucose must be infused intravenously at a rate of 250 mg. per 100 mg. of body weight per hour (Cori and Cori, *J. Biol. Chem.*, 1927, lxxii, 597). Hence, a mobilization of 750 mg. of liver glycogen or an initial glycogen content of the liver of 20 per cent is required, if the hyperglycemia of 174 per cent is to be explained merely on the basis of glycogen mobilization in the liver. Actually there were only 218 mg. or 5.6 per cent liver glycogen present to start with (Table II), and the liver glycogen showed an increase after the epinephrine injection. This indicates that other factors play a rôle in the production of hyperglycemia besides mobilization of liver glycogen. In fact the experiments with epinephrine in Table IV, when taken at their face value, give no evidence that liver glycogen is being mobilized; only by means of a finer analysis could it be shown that mobilization of liver glycogen occurs.

"Decreased utilization of blood sugar is one of the principal causes for the epinephrine hyperglycemia under postabsorptive conditions. The blood sugar rises after epinephrine injections, because the utilization of blood sugar in the peripheral tissues falls behind the supply of blood sugar by the liver, even if the supply is not much higher than normal. For this reason, amounts of sugar given off by the liver will cause hyperglycemia, amounts, which when injected into normal animals, have no effect whatever on the blood sugar level. Hitherto it has been assumed that a decreased utilization of blood sugar must be associated with a decreased carbohydrate oxidation. The present experiments reveal that after epinephrine injections carbohydrate oxidation is carried on at the expense of muscle glycogen and that the carbohydrate oxidation may be increased in spite of a diminished blood sugar utilization."

"The conversion of lactic acid derived from muscle glycogen into liver glycogen explains why epinephrine hyperglycemia can persist for several hours without causing depletion of the glycogen stores of the liver. A decrease in liver glycogen is to be expected only if glycosuria develops. In rabbits during epinephrine glycosuria more sugar appears in the urine than can be accounted for by the disappearance of liver glycogen, indicating that resynthesis of liver glycogen from lactic acid occurs also in this species (unpublished experiments). It can now be understood why different observers obtained conflicting results when they determined the glycogen content of the liver after epinephrine injections. With small doses of epinephrine, or even with large doses when the glycogen content of the liver is low, resynthesis of liver glycogen from lactic acid exceeds mobilization, and consequently the liver glycogen is found higher after the injection. With large doses and a high liver glycogen the latter diminishes because the loss of sugar in the urine can not entirely be compensated by resynthesis of liver glycogen.

"It is surprising that an extrahepatic action of epinephrine on carbohydrate metabolism has not been emphasized before. The experiments on 24 hour fasting and on rats in the postabsorptive state indicate that the extrahepatic action of epinephrine consists in a mobilization of muscle glycogen. Whether this mobilization is responsible for the decreased utilization of blood sugar, or whether both processes are influenced independently by epinephrine, can not be decided at present.

"Since the end-product of glycogen breakdown in the muscle is lactic acid, epinephrine can not raise the blood sugar level after removal of the liver. However, the influence of epinephrine on blood sugar utilization is demonstrable on hepatectomized animals, as will be shown in subsequent papers.

"Insulin produces hypoglycemia because the supply of sugar falls behind blood sugar

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utilization, in spite of a rapid mobilization of liver glycogen. Epinephrine and insulin antagonize each other on account of their opposite effect on blood sugar utilization in the peripheral tissues."

The experimental work showed that in control rats 216 mg. of glycogen disappeared in 3 hours time: 23 per cent was derived from the liver, 77 per cent from the rest of the body.

In animals injected with epinephrin all the glycogen which disappeared was derived from the body, the glycogen of the liver being actually increased. After insulin, 43 per cent of the disappearing glycogen was derived from the liver and 57 per cent from the body. The differences in carbohydrate oxidation were extreme and point to the great differences in action on carbohydrate of epinephrin and insulin. In comparison with the controls, epinephrin injection caused an increase in carbohydrate oxidation of 19.5 per cent and insulin, 97.3 per cent.

The so-called antagonistic effects of epinephrin and insulin on sugar metabolism are, in the light of the Coris' work, not antagonistic in the sense that one opposes the action of the other, for it will be shown later in this article that insulin very likely counteracts the action of epinephrin by synthesizing the precursor of glycogen which epinephrin breaks down. Cori and Cori, however, state that, "Whether or not these two hormones act antagonistically by influencing the same process in an opposite direction must remain undecided as long as the actual point of attack on the carbohydrate molecule is unknown. . . . ." "Insulin is the hormone that leads to a preferential utilization of blood sugar and indirectly of liver glycogen. The antagonistic action between insulin and epinephrine is explained by their divergent effect in blood sugar utilization."

Macleod (6) had predicted the same thing without the experimental facts later demonstrated. "Although in their effects on blood sugar, the two hormones may therefore be said to be antagonistic, it must be remembe that this may be of little physiological sig icance, and merely be due to the fact t insulin leads to the disappearance from t blood of the excess of glucose which epi phrin causes to be liberated from the liv just as it does when the excess of glucose absorbed from the intestine, or administer parenterally."

It has now been shown that epineph actually acts on muscle glycogen and t the increase in the blood sugar is due to t formation of liver glycogen from the lac acid derived from muscle glycogen. Blo sugar rises because the increased liver gl cogen gives some additional sugar to t blood and this accumulates due to a depr sion of utilization by the peripheral tissue The blood sugar is again available for use oxidations and in storage of glycogen in t muscles and the cycle is complete.

This "cycle of carbohydrates" with lac acid in the intermediary stage is based upo some of the soundest physiological researc A. V. Hill (7) has outlined series of chang taking place in muscle which his own researche and those of Meyerhoff and Fletcher a Hopkins have established. These chang studied in the complete absence of oxyg are as follows:

"(A) Glycogen disappears.

"(B) Lactic acid appears in equivalent amount.

"(C) Preformed CO_2 is driven off.

"(D) Heat is produced proportional t the lactic acid formed.

"(E) The hydrogen ion concentratio rises."

The part played by the lactic acid has bee described. Hill says that in the period o recovery (following the anaerobic phas above) oxygen must be taken in to provid the necessary energy. He describes the two phases in the recovery process. The first is the oxidative removal of lactic acid in t muscles where it was formed, and the secon is the removal of lactic acid which has b

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one to escape by diffusion into the blood. It is this part which escapes oxidation (with the consequent liberation of energy) that Cori and Cori describe as the precursor of liver glycogen and a link in the "carbohydrate cycle." These findings (in so far as epinephrin causes a decrease in muscle glycogen and an increase in liver glycogen) have recently been corroborated by Blatherwick and Sahyun (8) and by Himwich, Koskoff and Nahum (9) who also demonstrated the part played by lactic acid.

"The glucose and lactic acid content of the blood of twenty-nine amytalized and eleven decerebrate dogs was studied during rest and exercise. As indicated in the schema, a glucose-lactic acid cycle exists between muscle and liver. Lactic acid liberated from muscle finds its way to the liver through the blood stream, and is there converted to carbohydrate. The liver in turn yields glucose to the blood, thus affording a supply of carbohydrate to muscle.

Glucose

Liver ⟶ Muscle

⟵

Lactic acid

It must therefore become apparent that by virtue of this cycle, the liver becomes an integral part of the mechanism of recovery."

The part played by insulin seems in most respects opposed to that of epinephrin. Insulin acts by utilization of liver glycogen instead of muscle glycogen. It increases the peripheral oxidation of blood sugar as well as converts it into an unknown storage substance. In bringing about these effects it causes the withdrawal of liver glycogen which is converted into blood sugar. Liver glycogen is the only source of blood sugar and insulin acts both in the phase of liberation of glycogen and in the phase of utilization of the liberated dextrose.

In considering the action of insulin it becomes more apparent that glycogen is not a mere storage form of sugar but is in all probability an indispensable intermediary stage in the final utilization of carbohydrate in the body. Irrespective of its origin either from carbohydrate or protein (or possibly fats), it must finally be deposited in the liver to be available for formation of blood sugar. It has been suggested that this may be a necessary step because the dextrose which is formed from liver glycogen may be of a different type from the α-β-dextrose from which it is synthesized. In view of the unavailability of muscle glycogen it is possible that the glycogen synthesized in the liver is also of a different type than muscle glycogen. Glycogen is not well understood in its chemical characteristics. The evidence of a special form of "active" dextrose differing from α-β-glucose, which may be necessary before it can be oxidized by the body has been given in previous issues of the JOURNAL. Insulin may either be necessary for the formation of this special type of dextrose which can then be oxidized by the tissues, or it may require it, and no other type, in order to effect the oxidation. Another possibility may be suggested. Insulin may be necessary for the formation of a special type of glucose capable of being synthesized into the unknown substance (hexose phosphate?) which is a precursor of glycogen. The mechanism of action of insulin, however, on glycogen formation and sugar utilization is not understood. In diabetic animals insulin injections cause a disappearance of sugar from the blood by increased oxidation and an increased formation of glycogen. In normal (starved) animals, however, insulin inhibits glycogen storage, and in normal well fed animals it reduces glycogen. Macleod says that in normal animals the amount of free glucose in the tissues (tension of glucose) is reduced and sugar disappears from the blood: this disappearance is not due to a polymerization of glucose to glycogen or entirely to an increase in the relative amount of carbohydrate undergoing combustion. Macleod terms the condition which permits the relatively

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enormous removal of sugar from the blood, a "sugar vacuum" of the tissues. Experimental evidence is against the conclusion that the sugar disappears as a result of some sort of glycolysis in the blood itself, whereby the blood simply holds the products of sugar hydrolysis. Actually the experiments showed that the site of insulin action is in the cardiac and skeletal muscles and not in the liver. Since in normal animals the removal of sugar by insulin can not be accounted for by increased formation of glycogen or entirely by increased oxidation, the problem becomes one of accounting for the fate of the sugar. Macleod (9) accounts for it as follows:

"We believe by assuming that insulin stimulates the formation of some unknown substance which maintains a certain equilibrium with glycogen, and stands on the way between this and lactic acid. This unknown substance may be a stepping stone in the conversion of carbohydrates into fats, and it is possible that in its formation a phosphorous acid complex, such as hexose phosphate is involved."

In addition to this storage of blood sugar as glycogen or as an unidentified precursor of glycogen, there is an increased oxidation of carbohydrate following insulin injection. This is shown by an increased respiratory quotient and by an increased oxygen consumption. The extent to which it is oxidized, however, can not account for all the sugar leaving the blood. In diabetic animals the action of insulin is to definitely increase the oxidation of carbohydrates.

The possibility of some endocrine substance or substances secreted by the pancreas, other than insulin which might exert an influence on carbohydrate metabolism has long been a subject of speculation. Many experiments and clinical observations strongly suggest it. N. F. Fisher (10) reached the conclusion that "Insulin probably does not represent the entire pancreas hormone complex, since in the total absence of the pancreas insulin can not maintain life or does not control all the diabetic symptoms (subnorm... weight, polyphagia, polyuria)."

Chaikoff, Macleod and Markowitz (1... found that when insulin injections were s... plemented by daily feeding with raw pa... creas, dogs could be maintained in g... bodily nutrition and concluded:

"That the presence of something deriv... from the pancreas either its digestive f... ments or some internal secretion besid... insulin is necessary for the maintenance ... normal metabolism."

Recently, Ronzoni, Glaser and Barr (1... have demonstrated the presence in the pa... creas of a substance which exerts an inhibitory effect on glycolysis in muscle. They al... arrive at the conclusion that a hexose ph... phate (see Macleod's assumption above) ... a necessary part of lactic acid formation ... muscle. "In muscle extracts then the co... mechanism by which lactic acid is produc... is through the intermediary involving carb... hydrate and phosphate disappearance, pr... sumably hexosephosphate. Unless the mec... anism existing in muscle, frozen and hash... is different from that in muscle extract, th... is evidence that the preformed precursor ... lactic acid existing in muscle is a compl... involving carbohydrate and phosphate." The... work suggests that (at least in solution ... muscle extracts) carbohydrate combines wit... phosphate to form hexose phosphate and ... this compound is then broken down into lac... tic acid and phosphate. The inhibitor ele... ment of the pancreas acts on the phase of ... phosphate-carbohydrate formation—inhibit... ing the process of esterification and preventi... an accumulation of this precursor of lac... acid. The subsequent breakdown of th... ester (hexose phosphate) into phosphate a... lactic acid is not materially affected by ... inhibiting substance.

The knowledge of the opposed effects of ... pancreas internal secretion and epinephrin... on blood sugar has been largely extended. ... The following facts have apparently be... demonstrated. Both exert their action in t...

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peripheral tissues and not in the liver or on sugar in the blood. Insulin apparently stimulates the production of an ester or some unknown substance (probably hexose phosphate) and a pancreatic inhibitor substance retards it. This substance (hexose phosphate?) is a precursor of glycogen and doubtless stands in chemical equilibrium with it. A pancreatic inhibitor substance exerts an opposed effect and inhibits the synthesis of hexose phosphate. Epinephrin increases the mobilization (oxidation) of muscle glycogen and decreases the utilization by the muscles of blood sugar. The products of muscle glycogen splitting (lactic acid) are synthesized into liver glycogen.

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A Contribution to Kottmann's Reaction

(Translated from the article by Dr. Emil Walder, *Mitt. Grenzgeb. Med. u. Chir.*, 1926, 39 : 626, No. 4/5.)

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(CONTINUED FROM VOL. XIV, No. 2)

III. *Concluding Remarks*

In the work given before we have regarded the Kottmann reaction perhaps too much from the standpoint of pure colloid chemistry; in this we are, however, convinced that the colloid chemist himself would have proceeded still more critically. We drew attention to positive sources of error of the method and showed that the opinion of Kottmann that the degree of browning of his sera is a direct measure for its degree of dispersion or its dispersibility is not yet demonstrated, which moreover Prof. Kottmann acquiesced in an oral discussion. We showed that the relations between degree of dispersion and degree of browning are not of so simple a nature, and demonstrated in concrete examples, as Kottmann himself also says, that "profound investigations are still necessary to clear up the theoretical basis of the method in all directions" or, as it is reported later, "that without doubt the method is still further to be cleared up and in need of development in various points".

If we review the literature which has appeared concerning the Kottmann reaction, we must observe that certain authors who work with the method, perceive in it, as it were, a dispersometer for serum and in part on the basis of their results with the Kottmann reaction produced theories concerning physiology and pathology of the thyroid

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function, which, it appears to us, go somewhat too far. So, for example, says F. Starlinger ("Physico-Chemical Investigations on the Thyroid Problem," *Grenzgeb.*, Bd. 36): "And finally Kottmann offered his photoreaction, which properly first conceived the physical condition of the albumin colloid in the serum, so to speak, bodily . . .." That this physical conception of the albumin substance is still problematic we believe we have shown sufficiently. We do not wish to enter into this point, but permit ourselves several remarks on another declaration of Starlinger. In the same work, Starlinger says, in part on the basis of his results with the Kottmann reaction, that a task of the thyroid is to transform coarsely disperse albumin into finely disperse. A struma which does this is said to be hyperfunctional; on the other hand, the reverse is also said to occur, that, to be sure less frequently, the finely disperse serum appearing in the thyroid leaves it as coarsely disperse, "lowering of the plasma dispersion in venous blood characterizes the hypofunctioning goiter." A positive contradiction appears to us to be present here. A gland, which reverses its function on the contrary — which was the case in the hypofunctional struma, according to what was said above — does not seem to us to be hyperfunctional; in our opinion, it should rather be called "contrafunctional." That in general a gland can reverse its function to the opposite, seems explainable with difficulty. It is well known that there are ferments which reverse their effect from a certain concentration of the reaction product. That, however, a whole gland reverses its activity, falls out of the bounds of what is known up to the present. A gland can show hyper-, dys- or hypofunction. We do not, however, as yet know "contrafunction." If the normal or hyperfunctioning thyroid truly displays a dispersing activity for the serum, it must be assumed that the diseased, hypofunctioning gland does this in lessened measure or no longer at all. The border case would therefore be that in which a gland simply allows the blood to pass changed, so that the entering and leav plasma shows the same dispersion. O could only arrive at the Starlinger concep if one would make the auxiliary hypothe that the dispersion would be coarsened passage through any indifferent orga Points of support for such an assumption however not known to us. The difficul with the whole thing must lie elsewhe Before we can proceed with the solution such questions, we must have at our dispo methods which permit us to compare t degree of dispersion of the various sera o plasma, measured in absolute proportion, f from objection. This is, however, not yet t case. Aside from this we do not in gener know how the physical process of change o dispersion stands in respect to the chemic decomposition of the albumin molecul which seems to stand in the foreground i thyroid function. Increase in dispersi proves no albumin decomposition as ye although it can precede it. It is self evide that nothing is changed in the fundamenta question of an internal secretory process i the thyroid through these discussions con cerning the dispersion.

As far as the method is concerned, Sta linger also says that the values of the Kott mann reaction are of course to be realized with some precaution, since precisely wit this method the individual shades of colo present a rightly subjective factor. He pre vents the coagulation of the blood through th addition of citrate, in order to be able t determine the dispersion of the plasma; now we have already cited at the beginning of ou work the changes in color observed by Lüppo Cramer in the growth of gelatin-containin silver germs under the influence of phos phate or citrate. The possibility is suggested that also in the colloid silver arising according to Kottmann, the color changes may appear under the influence of citrate. One would accordingly first have to test the influen

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of the citrate experimentally. Whether the citrate is without influence on the dispersion of plasma we also do not know.

Still another brief remark on Starlinger's work. He says that the cubital vein blood serum on which the whole organism has finished working can not give any more enlightenment concerning the function of the thyroid. Of course, the thyroid secretion is very quickly changed in the living blood or organism as the most recent investigations show. The investigations of Hara and Branovacky show, however, that in pronounced functional disturbances it still remains biologically active. Our own investigations show the same thing. In our tables we also compare with each other venous blood sera from the arm in normal, exophthalmic goiter patients and cretins, in order to determine that in exophthalmic goiter the delay in reaction is definite and the degree of browning is a little less intensive. Moreover, Kottmann's investigations show this already, and he performed his reactions only with venous blood from the arm.

Another author, E. O. Schmidt ("Concerning Morbus Basedowi," *Grenzgeb.*, Bd. 33, 1921) used for the performance of the Kottmann reaction 5 per cent instead of 0.5 per cent solutions of potassium iodide and silver nitrate, subjected it to light with 200 candles for 10 to 25 minutes — at what distance he does not say. In this tenfold stronger concentration of the reagent probably the albuminous substances of the serum, in their function of dispersing agent, result in the ensuing colloidal silver iodide, and the silver is so strong in the background that quite possibly one sees a reaction totally differing from the Kottmann reaction. In so strong a concentration it is possible that most of the silver iodide formed does not remain as a colloidal solution, but instead precipitates out directly. Moreover, we have also referred to the fact that the result of the reaction is in high degree dependent on the amount of light which hits on every square centimeter surface of the reaction mixture; constance of light source, of distance of it from test tube and the time of lighting are, accordingly, absolutely indispensable in order to obtain reliable results comparable with one another. Schmidt has apparently had too little regard for these factors, for his results to be comparable with ours.

With this we have arrived at the conclusion and hope despite the criticism which we had to exercise on the Kottmann reaction — a criticism which does not refer to the clever basic idea of Kottmann concerning the realizability of which we have moreover no doubt, but refers to the present form of practical execution of his reaction and its significance — that we have shown that Kottmann has nevertheless through his method of serological thyroid examination shown a way which when once developed further, can bring valuable results to maturity.

Summary

1. The Kottmann reaction in the form described here for its practical execution, in so far as this may be judged from the cases investigated here, gives results in the sense that the sera developed according to it stain brown in varyingly marked degree; the most pronounced degree of browning is shown by the dwarf cretin sera; the weakest by the exophthalmic goiter sera; in between lie the sera of goitrous cretins, of ordinary goiters and the normal sera. The goiter venous blood sera show in general less marked degree of browning than the venous blood sera from the arm. The degree of brown coloration may be related more or less well (with several exceptions) with the clinical picture of the case in question.

2. If we disregard dwarf cretin sera and severe cases of exophthalmic goiter, the differences in degree of browning between the individual maximal developed sera are not very great.

3. These degrees of browning were measured on a Kollargol standard which remained constant for this.

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4. Concerning the relation between degree of dispersion and degree of browning there are not as yet any experimental investigations; Kottmann's opinion that the browner a serum developed by his method is, the more coarsely disperse its micelles, is accordingly not proved. The conditions seem to be quite complicated here.

5. Essential sources of error are connected with the Kottmann reaction, which are conditioned by the capriciousness of the silver iodide and of the colloid silver, with respect to their color and degree of dispersion.

6. The sequence of addition of the reagents, the type of light, are of great influence on the result of the reaction; a constant technique strictly adhered to in experiments is accordingly an unconditional requirement in the execution of the reaction.

Practical Therapeutics

High Blood Pressure

THE intense interest displayed in recent years by profession and laity in high blood pressure is not of itself evidence that this condition is more frequent than formerly. The development of the clinical sphygmomanometer with the consequent ease in estimating blood pressure, the increased publicity given to life insurance and public health and mortality records, have all served to fix attention on this rather widespread condition of pathological physiology.

Hypertension is doubtless a precursor of arteriosclerosis and of general cardio-vascular disease but it is frequently, perhaps usually, found unassociated with these conditions. When associated with arteriosclerosis, however, the term "essential" hypertension is commonly applied.

The symptoms of arteriosclerosis, therefore, are chiefly the symptoms of the hypertension.

Toxic conditions have received much attention as a cause of hypertension and of arteriosclerosis, and it seems likely that a common toxic factor is the cause of both. Foci of infection, teeth, tonsils, chronic appendix, etc., metabolic diseases giving rise to toxic products of metabolism, have been related to both the arterial hypertension and the arterial changes. Obesity and diabetes likewise seem causative and suggest a toxic factor. Hartman and Ghrist (1), in a study of 2,04[illegible] cases taken from the records of the Mayo Clinic, found, "The inconstancy of the diastolic readings emphasizes only the striking constancy of increase of systolic blood pressure with increasing weight in a non-selected group of office patients in a general practice."

In an exceedingly enlightening paper Blackford, Bowers and Baker (2) have shown the strong family tendency of this condition, its incidence after 50 years of age and its tendency to persist. They have analyzed the histories of 222 of 401 patients who were examined from 5 to 11 years ago. Their conclusions are:

"A study of 401 hypertensive patients (systolic pressure 175 or over) found in 10,000 clinical examinations made in a general clinic from five to eleven and one-half years ago has shown that:

"1. The appreciable incidence (1.2 per cent) of hypertension begins in the fourth decade; 5.8 per cent of all patients examined in the fifth decade showed hypertension, 12.3 per cent in the sixth, 22.5 per cent in the seventh, 14 per cent in the eighth, and 10 per cent in the ninth showed blood pressures above 175.

"2. Sixty-five per cent of the hyperten-

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sive cases in this series are in women; 50 per cent of all patients examined were women.

"3. The remarkably greater number of women having hypertension, as compared with men, comes in the fifth, sixth, and seventh decades.

"4. Family histories of hypertension were noted in more than one third of all histories.

"5. Cases of hypertensive disease complicated by goiter, syphilis, diabetes, chronic nephritis and valvular heart disease have each shown by groups no particular difference from cases of pure hypertension.

"A follow-up study of 222 of 401 hypertensive patients (55 per cent) examined from five to eleven and one-half years ago has been made. Twenty of these have been discarded for statistical study because they were moribund at the time of examination or died shortly afterward from other diseases. The 202 cases remaining, followed from five to eleven and one-half years, have shown:

"1. A gross mortality of 50 per cent, a male mortality of 70 per cent and a female mortality of 39 per cent.

"2. A mortality about the same for moderate and marked cases, but twice as high in extreme cases.

"3. An average duration of life after the first observation of thirty-two months for males and forty-four months for females.

"4. An average time since the first examination of 101 living patients of eighty-one months.

"5. Known causes of death, thirty-one from cerebral complications, twenty-five from heart disease, eighteen from uremia.

"We have not found any tendency toward recovery in hypertension.

"Occasionally remarkable exceptions are seen to the general rule of mortality. Women with hypertension sometimes outlive their expectancy. Men almost never do."

The treatment of hypertension falls under the general headings of hygiene, dietary and drug. O'Hare (3) says, "The care of such a patient should be based primarily on the knowledge that the problem is that of a generalized circulatory disorder consisting essentially of a functional vaso-constriction at first, then a more or less progressive small blood vessel sclerosis with superimposed vaso-constrictions, and finally as a result of cutting down of the blood supply to various organs, secondary degeneration and impaired function of these organs."

Rest, freedom from heavy muscular exertion, warm baths, mud baths, light treatment and the cultivation of habits of repose and efforts to relieve a tendency to worry are valuable. Excessive expenditure of nervous and physical energy should be guarded against. Diet, as a rule, is simply arranged by reducing the intake of food down to the energy requirement of the patient. In the overweight patient, reduction of diet and restriction of carbohydrates and fats are important.

For drug treatment, sodium and potassium iodide is classic. In cases with a history of syphilis they are valuable. Amyl nitrite by inhalation is valuable in controlling the sudden increases of pressure so frequently encountered. Nitro glycerin U. S. P. 1 minim by absorption from the mouth is to be used for the same purpose. Potassium sulphocyanate and bismuth subnitrate have recently received attention.

"Chemically pure potassium sulphocyanate was prescribed in a simple aqueous solution of such strength that 1 fluiddrachm (4 cc.) contains 1½ grains (0.1 gm.) of the salt. This dose was given in water by mouth three times daily, after meals, for the first week, twice daily for the second week and thence once daily for the third week of treatment. Thereafter this dose was given daily, or every other day." (4)

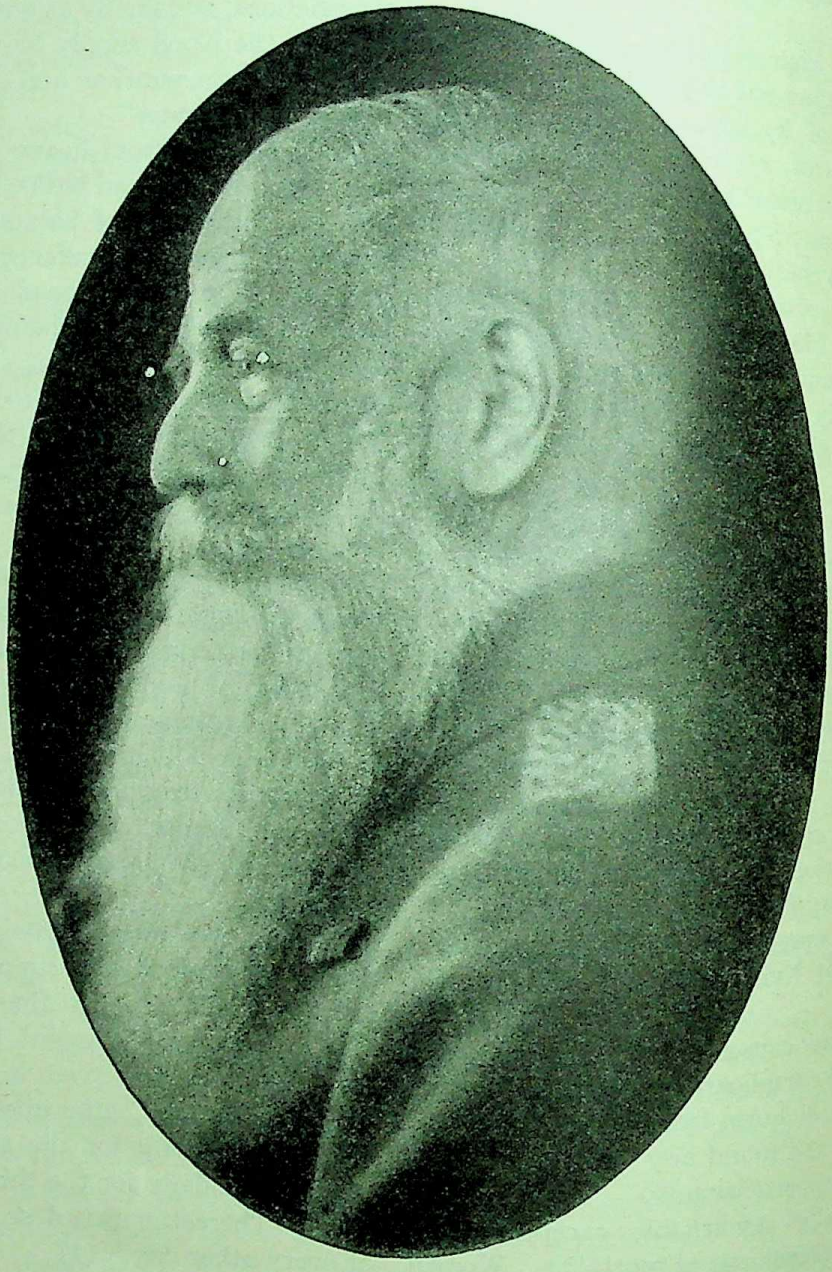
Bromides and luminal are most helpful in some cases characterized by nervous irritability. The effect of bismuth subnitrate on hypertension has been carefully studied by Stieglitz (5) who suggests the probable mech-

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The Doctor's Page



ARTHUR HARTMANN

(1849-)

The opportunity is not given to every one to serve his country in two wars and in a long interim between, to devote himself to successful private occupation so commendable as to obtain for him the highest honor of his state. In this respect Arthur Hartmann is unique.

He was born on January 1, 1849, in Heidelheim, a city situated near the eastern bord-

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of Württemberg. His early life was uneventful. In Heidenheim and later in Stuttgart he received elementary and intermediate education, and at the age of 18 he sought entrance to the University of Tübingen for the purpose of studying medicine. After a little more than two years here his studies were interrupted by the war of 1870-1871, for he entered the military service as assistant physician in the Third Württemberg Field Hospital.

After the war Hartmann resumed studies at Freiburg and then at Leipzig, and in 1873 he was graduated from Leipzig. A brief activity as army physician occupied him until he undertook a journey to England, where he became acquainted with Lister, and to France. The years 1875 and 1876 Hartmann spent in Vienna studying especially diseases of the ear, nose and throat and after this extended period of preparation, in which he availed himself of much practical application he ventured definitely to set himself up as a doctor of diseases of the ear, nose and throat in Berlin (1876). The fact that he was found still practicing in Berlin 35 years later is meritorious. Excellent training in his subject and accurate diagnosis of the material presented soon won for Hartmann a reputation, not only in Germany but in other countries as well.

In order to satisfy an inclination to teach, Hartmann founded a polyclinic, where, from 1881 to 1894 he gave courses in his special subject. These lectures and classes were attended by physicians from all parts of the globe, who were desirous of acquiring the excellent technique of this man and of benefiting from the profound researches he carried on. In 1902 the title of Professor was bestowed upon him, in honor of his distinguished service. When the Rudolf Virchow Hospital was founded in 1905, Hartmann was called to the post of directing physician of the department of Diseases of the Ear, Nose and Throat. In 1909, his honorary titles culminated with that of *Geheimer Sanitätsrat*, the highest he could achieve. The following two years were crowded with much activity in his special field, and then he settled down for a well earned rest in his native city, Heidenheim. He turned his attention to social service, becoming the Director of the Society for the Improvement of Heidenheim; as an outgrowth of an interest in Uhland, he published a popular book referring to this locality and held a very successful exhibition of Uhland material in Tübingen. He was also identified with activities intending to curb the use and sale of alcoholic beverages in his province.

It was not long, however, before the tranquillity of his life was interrupted by the World War. He again entered the service of his country in medical capacity. In the early part of the conflict he was head physician in a hospital train, and later, though he had already led an active life passed his 65th year, he took charge of a reserve hospital until the end of the war.

Hartmann has contributed a great deal to the service of mankind, in his practice by the judicious application of knowledge gained from accurate pathological, anatomical and clinical investigations and by recording his findings in numerous scientific publications. Many of his writings, of which the greater part is composed of books or monographs, deal with diseases of the ear, nose and throat, and especially with deafness and dumbness and the education of the deaf and the dumb. Some of these are *Experimental Studies on the Function of the Eustachian Tubes* (1879), *Deaf-dumbness and the Education of the Deaf and Dumb* (1880), *Diseases of the Ear and Their Treatment* (1881) The success and reliability of the last two books have been so great as to more than justify their republication and translation from German into other languages. *Atlas on the Anatomy of the Frontal Sinus* (1900), *Textbook for the Instruction of the Deaf* (1909), *The Deaf Individual in the School* and *The Education of the Totally Deaf in Germany* (1912) render evidence that Hartmann not only treated his patients but also followed up with more permanent aid to those particularly afflicted with the handicaps of deafness and dumbness.

Hartmann broadened the scope of his literary activity when he took charge of the publication of *Zeitschrift für Ohrenheilkunde* after the death of Professor Moos. For a number of years the *Vierteljahresbericht* prospered under his expert supervision. From 1900 to 1904 he edited the *Verhandlungen der Deutschen Otologischen Gesellschaft* and became its President in 1906. Recently Hartmann has been attracted to the subject of nutrition and published, in 1928, a volume on *Nutrition and Raw Diet.*

During his active scientific career Professor Hartmann was interested in all things medical

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Medical Subjects by Famous Masters



"THE MONKEY DENTIST," by Michel Marie Charles Verlat (1824-1890)
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Editorial Comment

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Crystalline Ovarian Hormone

SINCE the preparation by Allen and Doisy of solutions containing the active estrus-producing hormone of the ovary, the activity of which was demonstrated by the vaginal smear method, there has been widespread activity in attempts to isolate the hormone as a pure crystalline substance. It is true that active extracts had been prepared before Allen and Doisy but they were of uncertain strength; the methods of preparation were complex and uncertain and there was no way of standardizing them or of comparing their values. The "lipoid" character of the ovarian hormone was first demonstrated by Iscovesco and his 11 Fb and V Dc, soluble in ether and alcohol, were among the best known preparations 15 years ago.

Seitz, Wintz and Fingerhut, Aschner, Frank, Rogers, Fellner, Herrmann and others made extracts of varying activity in the early period of study. The method of assay was more in the nature of a qualitative test — the effect on hypertrophy of uterus and tubes, on animal behavior, etc.

The introduction by Allen and Doisy of the Papanicolau-Stockard method of determining estrus by the vaginal smear method in 1923, made precise valuation possible and contributed enormously to all succeeding research.

The oily (lipoid) character of these preparations was a decided disadvantage and necessitated either the use of a bland inert oil for injection or the use of a colloidal aqueous solution.

Further research made clear, however, that although the active principle was extracted with lipoid solvents and was apparently itself a lipoid, it was possible to split the hormone from the oil and make a true water solution. Zondek, Laquer, Dickens and Dodd have been able to prepare these water-soluble preparations.

The estrus-producing hormone (as distinguished from the inhibiting hormone of the corpus luteum) may be obtained from the liquor folliculi of the ovary, from the placenta, from the blood, and from the urine of pregnant women.

Very recently Doisy, Veler and Thayer (1) have prepared the hormone in crystalline form.

"A crystalline product which has been recrystallized several times has been isolated from the urine. The assays show that the crystals are physiologically more active than any preparation obtained thus far, the activity being more than 2000 rat units per milligram."

This work of Doisy and his associates confirms the opinion of others that the principle obtained from liquor folliculi and the urine is the same. In the *Lancet* of January 4, 1930, it is reported that Dr. Butenandt of Göttingen has also produced a crystalline ovarian hormone.

"Butenandt worked with an oily material which was obtained from the urine of pregnant women, and contained about 30,000

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mouse-units per gramme. By repeated distribution between two solvents (aqueous alcohol and petroleum ether) inactive substances were removed in the petroleum ether fraction, and the material then had 500,000 mouse-units per gramme. This substance was further purified by the use of other solvents (ether, benzene, and ethyl acetate) and by adding alkali in increasing strength to the acid solution. An alkali-soluble fraction was obtained which had a mouse-unit of only 1.5 to 2 millionths of a gramme. Further purification was effected by distilling this oil in a vacuum of 0.20 — 0.03 mm. Hg and at a temperature of 130 — 150° C., and the material then contained 5,000,000 units per gramme. Sublimation in a high vacuum or treatment with solvents yields a crystalline product of which one gramme contains 8,000,000 mouse-units.

The development of a crystalline hormone of such astonishing potency is interesting in view of the lack of effects found by Frank at Mount Sinai Hospital, New York, in the case of practically all of the best known commercial products of a "purified" and "concentrated" estrous hormone.

The field of application in practical medicine of such a product is not yet demonstrated. Novak has pointed out the fundamental biological differences between estrus in lower animals and menstruation in the human female. Evolution has changed the process and altered the values of the several elements active in producing menstruation. In the human female the usual menstrual mechanism is greatly dependent upon the corpus luteum although the follicular hormone is, of course, important. Some cases may be observed in women in which there is a persistence of the more primitive follicular type of menstruation, but in general, human menstruation is not solely dependent upon the follicular hormone and it is not to be expected that this hormone alone will suffice in the treatment of irregularities of menstruation.

1. Doisy, E. A., Veler, C. D., and Thayer, S., *Am. J. Physiol., Abst.*, 1929, xc, 329.

Abstracts

The Ovarian Hormone and Its Site of Development. — W. Lahm. (*Zeitschr. ärztl. Fortbild.*, **26** : 78, 1929.)

The ovary accelerates ossification, controls sexual life, hair and growth of beard, development of baldness, pigment metabolism, tonus of the blood vessels, metabolism in the capsular ligaments (arthritis ovaripriva). Primary agenitalism is combined with hypotonia. In the climacteric the ovarian deficiency causes hypertonia. The generative function might also be the object of certain internal secretory relations. The most recent experimental investigations favor the idea that the disintegration of the ova and their resorption excite vegetative impulse. The substances which induce the growth impulse in the uterus — ovarian hormone — were originally obtained from the ovary. Today we know that numerous albumin substances, histamin, etc., can exert a growth stimulus on the uterus. The following requirements were set for the ovarian hormone: lipoid solubility, indestructibility (indestructibility even through digestion), specific activity, preparation from ovary, placenta, blood or urine.

Hypoglycemic Action of Combined Borate and Insulin. — Loeper, Ravier and Tonnet. (*Progrès méd.*, **47** : 189, 1929.)

The authors undertook experiments on four diabetic patients. Their blood sugar varied from 2 gm. to 3.50 gm. The patients first received injections of pure insulin; to the second injection, 0.45 or 0.90 sodium borate was added. In two cases the strengthening of the insulin effect and the reduction of sugar excretion through the combination with sodium borate were evident. In one case the inverse effect occurred: the combined injection had less of an effect than pure insulin injection.

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Concerning the Hormonal Therapy of Ovarian Hemorrhages. — Kraul. (*Wien. klin. Wochenschr.*, **42** : 158, 1929.)

Demonstration of a series of youthful patients in whom transfusions of 100 to 150 cc. of blood of pregnant women were undertaken on account of profuse, irregular hemorrhages, after styptics, curettements and irradiation of the spleen had remained without effect. Kraul considers the action of injections of blood of pregnant women to be the result of the hormone content of the pregnant blood, in favor of which the lasting success of the treatment also speaks.

Hypogenitalism. — Serdukoff. (*Progrès méd.*, **21** : 901, May 25, 1929.)

By hypogenitalism is meant the various endocrine disorders intimately connected with decrease, disappearance or absence of the genital glands. In women, the period of puberty and that of the menopause may be regarded as the manifestations of a physiological hypogenitalism; just as there are endocrinopathies with distinctly pathological tendency such as chlorosis and eunuchoidism.

Chlorosis is one of the affections observed exclusively in girls at the time of pubertal development. This condition is intimately connected with the decrease in internal secretion of the ovaries or with the delay in formation of the endocrine products of these glands. The greater number of symptoms of chlorosis indicates hyposecretion; certain ones may be explained as being the result of an autointoxication due to dysfunction of the endocrine glands. Chlorosis is regarded as a pluriglandular affection: in addition to the ovaries, the thyroid and pituitary are also involved.

In the amenorrheic forms of chlorosis good results of treatment are obtained by different organotherapeutic preparations extracted from ovarian substance, especially in combination with iron. In the menorrhagic forms it is logical to prescribe preparations of pituitary. In general medical treatment should be associated with regulation of living conditions and principles of general hygiene to aid the organism in the critical time of puberty.

Individuals are designated as eunuchoids who give the impression of castrates, even though their genital glands have not been extirpated. The genital insufficiency to which the various forms of eunuchoidism are related may present a symptom complex identical to that arising after complete ablation of the genital glands. Congenital or natural eunuchoidism is the result of congenital aplasia of the sexual glands; there are also atypical forms of eunuchoidism. From the clinical viewpoint in women totally castrated a characteristic symptom complex develops: menstruation is arrested. Later there appears atrophy of the mammary glands, of the external genital organs and of the uterus. There is retardation of development of the bones of the pelvis and of the lower extremities in the castrated woman. General appearance changes and the patients acquire masculine traits. Then, as result of the lack of endocrine influence of the ovaries, vasomotor, secretory, emotional and psychic disorders develop. There is also observed disturbance of general metabolism. The post-operative disorders are not so manifest after castration of mature women. Congenital eunuchoidism is rare. The symptoms of eunuchoidism correspond to those observed in castrated women: osseous modifications as well as absence or total disappearance of hair; menstruation is missing in typical cases; sexual desire is wanting.

Eunuchoidism is intimately related to deficiency of function of the genital glands. Among the number of etiological causes there is admitted emotional shock during intrauterine life. Traumatisms, infections and septic affections with destruction of the parenchyma of the genital glands may be related among the principal etiological causes of the late secondary forms of eunuchoid degeneration.

The differential diagnosis of eunuchoidism does not present any great difficulties in typical cases with definite symptom complex. The results of treatment are variable according to whether ovarian tissue capable of functioning is present or not. Most frequently treatment is symptomatic. Organotherapy may be applied by mouth or in injections; various ovarian preparations being used. In general, injections are most recommended. In certain cases of hypogenitalism and in particular in certain forms of hypoövarianism and eunuchoidism, there is noted decrease in sexual desire. In these cases associated treatment (ovarian preparations and yohimbin) is recommended. In cases where the symptoms of hypogenitalism are especially marked in the osseous system, it is good to apply combined treatment with ovary and calcium. In cases where primary lesions

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of the genital glands are associated with pluriglandular disturbances, treatment with thyroid or pituitary must be associated with ovarian treatment.

When eunuchoidism in women is accompanied by obesity, loss of hair and modifications of metabolism with retardation of the process of oxidation good results may be obtained with treatment by minimum or moderate doses of thyroid. In certain cases the symptoms of obesity psychic apathy, intellectual indifference, weakness of memory, muscular fatigue, fall of hair yield to associated treatment with the three principal glands of the organism: ovary, pituitary and thyroid.

In cases of total absence of the genital glands, after castration or in congenital eunuchoidism, the modifications assume so tenacious a character that treatment with simple or complex endocrine preparations remains unsuccessful.

The most real method of treatment at the present time applied to cases of eunuchoidism hypoövarianism and other forms of the hypogenital syndrome is the transplantation of endocrine glands. The transplantation of genital glands in eunuchoidism (homo- or hetero-transplantation) produces a good stimulatory effect. The transplantation often contributes to the arrest of atrophic processes of genital involution in the case of secondary eunuchoidism. In the primary forms of genital eunuchoidism transplantation of the ovaries relieves the painful nervous, vasomotor, psychic and somatic symptoms.

Hyperthyroidism Evolving towards Hypothyroidism in the Course of a Treatment with Iodin. — L. Dautrebande. (*Presse méd.*, **37** : 721, June 1, 1929.)

The author reports a case of a young man of 20 years with goiter and hyperthyroidism which was transformed into hypothyroidism during an iodin treatment. He calls attention to three interesting points in this clinical observation: (1) a definite case of hyperthyroidism may be transformed into hypothyroidism under the influence of iodin. The author observed another case where the metabolism fell from +10 to −11 after 3 weeks of treatment and rose again immediately afterward. With Lemort, he also observed a third case where the hypothyroidism attained −20 per cent but was transient. This is the first time, the author believes, that the appearance of a prolonged hypothyroidism following administration of iodin has been reported. (2) The second interesting point is a change in the exterior appearance and intellectual habitus of the patient during the treatment. This change is paradoxical as the patient observed distinct signs of cretinism disappear at the time when his metabolism had been below normal for several weeks. (3) Finally a third point of this case report is worthy of mention: the coincidence of a definite hyperthyroidism with a soft goiter without nodules appearing clinically as a simple colloid goiter of adolescence and the transformation of this simple hyperthyroid goiter into a hard adenomatous protuberant goiter contemporaneous with a hypothyroidism, whereas this type of hard goiter is frequently the accompaniment of toxic hyperthyroidism.

Clinical examination alone is not sufficient for drawing a conclusion of hyperfunction or hypofunction of a thyroid; determination of the basal metabolism remains the indispensable diagnostic aid.

Further Investigations in the Preparation, Biology and Clinic of Pituitary Anterior Lobe Hormone. — B. Zondek. (*Klin. Wochenschr.*, **8** : 157, 1929.)

The anterior lobe hormone is a very sensitive substance which in contrast to folliculin is destroyed by cooking, acids and alkalis. Whereas folliculin is soluble in ether, anterior lobe hormone is insoluble in the majority of lipoid solvents, so that (for example in the preparation from urine of pregnant women) a separation of the two hormones is possible thereby. In the preparation of the hormone from the pituitary anterior lobe, placenta and pregnant urine, results are least objectionable and the gain is better by the way of precipitation which the author uses for the past 1½ years. It could be determined that pituitary anterior lobe hormone is precipitated under certain conditions through a series of organic solvents miscible with water (for example, ether, alcohol, methyl alcohol, acetone, etc.).

With dissolution of the precipitant in water there remains an insoluble residue which does not contain the hormone, so that in this way also a further purification is possible. The desiccated substance remaining, containing the hormone, is soluble in water.

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The author's investigations were undertaken on sexually mature (1600 to 1800 gm. weight) animals, as well as infantile animals (1100 gm.). Following 10 to 14 days of treatment (2 to 4 cc. pituitary anterior lobe extract equals 60 to 120 rat units *pro die*) there was shown a powerful influence of pituitary anterior lobe extract on the genital apparatus. The uteri had been transformed from thread-like tubes to formations as thick as one's finger (blue-red, livid in color) which contract immediately upon the stimulation of opening of the abdomen. In infantile animals one had the impression of a young pregnancy. The ovaries, of the size of lentils, became almost as large as cherries, replete with blood dots and golden yellow corpora lutea. Sections through the vagina showed less changes of the mucosa, especially increase in thickness of the vaginal musculature. The uterus showed this growth under the action of pituitary anterior lobe in still more pronounced degree. Here especially the markedly polypous proliferated uterine mucosa is conspicuous which is quite similar to a pregnancy mucosa in the rabbit. In the ovary the primordial follicles are displaced on the border zones in consequence of blood-filled luteinized follicle, in which in addition to the granular proliferation, the splendidly developed theca must especially be referred to. In the discussion, Aschheim could demonstrate the isolated, partly luteinized theca proliferation in the mouse under the action of pituitary anterior lobe.

The author knows little concerning the clinical action of pituitary anterior lobe extract in human beings, since he has used it only for the past ¾ year in the clinic.

Clinically the author was able to determine that anterior pituitary intramuscularly injected has a marked hyperemic influence on the female genital apparatus so that a picture of a young pregnancy can be simulated by turgor and color. This action determined through direct contemplation in operations he found corroborated thermometrically. The author was able to determine a rise in temperature of the peritoneum, which lay not as usual at 0.5°, but up to 1° above the axillary temperature. This pelvic hyperemia can doubtless be utilized clinically. Following a suggestion of P. Klein anterior pituitary extract is being used by the author in the University Clinic for Women of Charité, Berlin, in inflammatory pelvic affections in women, in order to induce the therapeutic effect through the hyperemia.

Through pituitary anterior lobe extract a stimulus to ovarian function in women is exerted and through it secondarily on the structure of the uterine mucosa. If one injects pituitary anterior lobe extract from the first day of menstruation to the eighth day of the cycle and then examines the uterine mucosa, a structural stage is found in this, which corresponds to about the 14th to 16th day of the cycle, the beginning of the secretion phase.

Concerning the Influence of Thyroxin on the Metabolism of Surviving Tissue. — K. J. Anselmino, O. Eichler and H. Schlossmann. (*Biochem. Zeitschr.*, **205** : 481, 1929.)

The reports in the literature concerning the action of thyroid hormone on respiration and fermentation of surviving cells are contradictory. The results of experiments which the authors carried out showed as the most striking change the increase of anaerobic glycolysis of the kidneys.

In sections of spleen, liver and kidneys of white rats 24 hours to 7 days following injection of thyroxin only a very slight or no increase in respiration was found, measured by means of Warburg's method. The anaerobic glycolysis of the kidney increases all the higher the stronger the increase of consumption of oxygen effect in the living animal through the thyroxin. The anaerobic glycolysis of the liver and spleen is not increased. The experiments prove that the thyroid hormone attacks the anaerobic phase of the metabolism in the first place.

On the Female Sex Hormone. III. Contribution. The Activity of the Estrous Hormone by Oral Administration. — F. Lange and W. Faure. (*Deut. med. Wochenschr.*, **52** : 310, 1926.)

With the value determination procedures given by the authors, it can be shown for the mouse by clear estrous cycle curves that the ovarian hormone is also effective by oral administration. Approximately a twenty times greater amount is needed, however, *per os*, than is effective subcutaneously. Important conclusions may be drawn from this experience for therapy. The active value of the best ovarian preparation for oral administration tested, was never over one mouse unit per single dose. If a mouse unit

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is placed as a basis for the assigned requirement *per dosis*, the authors calculate that 500 dragees *per diem* would be required for a preparation. However, the question whether a mouse unit will be sufficient to attain an effective amount of hormone in the organism, is more than questionable on the basis of experiments on rats (five times heavier in comparison with mice). From determinations on the blood of women, it could be calculated that 50 to 150 mouse units circulate in the total amount of blood. If we estimate at 1 to 2 days the duration of the effect with the unusually stable ovarian hormone, that amount must be given in this period (through substitution therapy in deficiency of ovarian function) which takes into consideration the fact that only 1/20 of the hormone value comes to active development by oral administration.

The Content of the Human Pituitary in Melanophore Hormone. — K. Ehrhardt. (*Münch. med. Wochenschr.*, **76** : 321, 1929.)

The author examined 50 pituitaries of human corpses in order to test whether that agent which brings the frog melanophores to expansion (melanophore hormones) is regularly contained therein. The results of investigation are: (1) The melanophore hormone is almost regularly contained in the human pituitary (in 48 of 50 cases examined). (2) The melanophore hormone is also visible in the pituitary of old people and of the newborn. (3) The melanophore hormone was missing in the pituitary of a patient who died of paralysis and in a patient whose autopsy showed typical Laennec liver cirrhosis.

In conclusion, the author states: there exist in adolescence and even in childhood pituitary adenomas amenable to radiotherapy. When they are accompanied by osseous lesions which characterize gigantism or acromegaly, their diagnosis is easy. In the absence of osseous lesions and especially with symptoms of infantilism, the differential diagnosis between these adenomas and tumors of Rathke's pouch offers great difficulties. In doubtful cases when radiography of the skull does not reveal supra- or intra-sellar calcifications considered to be pathognomonic of tumors of Rathke's pouch, the possibility of adenoma must be thought of and radiotherapy be resorted to, at least as trial, to replace it by surgical treatment as soon as aggravation of symptoms principally of visual disorders, shows the ineffectiveness of this test.

Organotherapy in Cancer. — Rous, Sergent. (*J. praticiens*, **43** : 319, 1929.)

According to the few observations reported by Naamé the idea should not awaken in physicians that organotherapy in cancer can play a rôle as active treatment. The observations reported merely show that the general condition of the patient was improved. It would be inadmissible to speak of a cure. Moreover, Sergent was never able to observe improvement in the anti-cancer center of Villejuif; he does not mention recoveries observed such as those reported by Naamé.

Pituitary Adenoma of Adolescence and of Childhood Amenable to Radiotherapy. — A. Béclère. (*Rev. neurol.*, **1** : 463, No. 3, Mar., 1929.)

Gigantism and acromegaly either associated or isolated are the clinical manifestations of chromophil adenomas. Gigantism always begins before the age of 20 years, either at the beginning of adolescence or often from childhood, sometimes before the period of puberty and sometimes after it. Such was the case of a young girl of 16½ years in whom the author obtained the first lasting success with radiotherapy. This was 20 years ago and results have been permanent.

The form which is principally ophthalmic with or without symptoms of hypopituitarism, is the clinical manifestation of chromophobe adenoma. Dott and Bailey report in detail the observation of a chromophobe adenoma of adolescence with partial infantilism erroneously diagnosed as a cyst of Rathke's pouch, operated by transfrontal route with considerable improvement of the vision and irradiated later.

In some cases of gigantism the syndrome of infantilism is more marked and more completely simulates the clinical picture of tumors of Rathke's pouch. Finally among the observations of pituitary tumors more or less improved by radiotherapy, which Dr. Sch... reported to the International Neurological Congress in 1928, three concerned children from 11 to 12 years.

Precocious Glandular Obesity with Optic Atrophy. — F. Terrien, H. Schaeffer and J. Blum. (*Rev. neurol.*, **1** : 798, No. 5, May, 1929.)

The patient, a child of 5 years, weighing 32 kg., presented bilateral optic atrophy with

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white papillae and excessive obesity, involving the trunk and members, but predominating at the pelvis, buttocks, pubis and lower members, whereas the face, neck, feet and hands seem almost immune, as in the adiposogenital syndrome. This child presents a bilateral cryptorchidism; the sella turcica is abnormally enlarged; the thyroid seems small. There is no neurosomatic sign; intelligence is normal. Wassermann reaction is negative in the blood. The obesity and blindness seem to have developed parallel from the first months of life. In this case the author questions whether the optic atrophy is dependent upon the chiasmatic compression by a pituitary neoplasm or if the blindness and obesity do not arise from the same heredosyphilitic cause.

Studies on the Influence of Substitution in the Thyroxin Molecule on the Action of Thyroxin. — Abderhalden and Werthheimer. (*Zeitschr. exp. Med.*, **63** : 4-5, 1929.)

Closely related combinations of thyroxin were tested for their action with respect to the development and growth of tadpoles and axolotls as well as for gas metabolism in rats. On the whole fourteen combinations were tested. In the first place the problem is to determine definitely whether the specific action of the thyroxin bound to the iodid atom in the molecule, either wholly or in part by Cl or Br, could be substituted. The de-iodized thyroxin proves inactive in substitute combinations, a fact of particular significance, in general it proves active when in higher concentration. This holds good even for di-iodid thyroxin, that is after cleavage of one iodized oxy-phenyl group of the thyroxin. There is naturally, the possibility that the substitution product of thyroxin in the organism will be changed back; it is also possible that the action of thyroxin itself is not strongly specific.

Concerning the Biology of Placenta Extract. — Gräfenberg. (*Klin. Wochenschr.*, viii, 1376, 1929.)

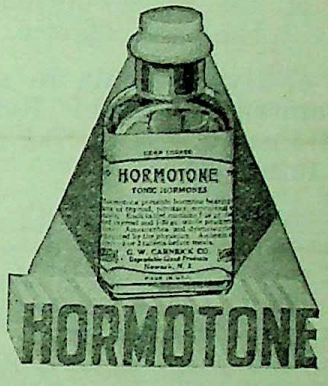
Injections of placenta extract into animals gave a negative Allen-Doisy reaction. In human beings in which an injection is justified following hemorrhage in pregnancy, they have a diagnostic value. Placenta extract works favorably in the interruption of internal secretions.

Of Course the Patient Came Back

The young woman with dysmenorrhea who receives palliatives will return, because the disturbance of menstruation is still present. But sooner or later she "tries" another physician. Endocrine therapy which gradually relieves the pain by correcting the faulty menstrual process makes a favorable impression on the patient and her family.

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Atrophy of the Genitals and the Hormone of the Anterior Lobe of the Pituitary. — K. Erhardt. (*Münch. med. Wochenschr.*, **76**, No. 30, 1929.)

During a ten months observation of the blood and urine of a 35 year old patient with intense atrophy of the genitals and chronic paranoid mental disturbance, there was found a permanent positive reaction to the anterior lobe of the pituitary. In contrast to this very rare case, the next almost inexplicable observation is a relatively frequent transient positive reaction to the anterior lobe. This was found, though in no way regularly, in women castrated by means of the X-ray and in totally extirpated women, in cases of genital carcinoma, uterus myomatosus, epithelioma of the chorion, acromegaly and pituitary tumor, at the beginning of the menopause and in climacterium praecox, in amenorrhea, lipoid kidney and after the transfusion of 500 cc. of blood from a pregnant woman. On the basis of over 300 cases (experimental results of 2000 tests) the reliability of the Zondek-Aschheim pregnancy reaction has been confirmed.

Attack of Hypersomnia in a Patient with Thomsen's Disease: Remarkable Action of Insulin. — J. A. Barre. (*Presse méd.*, **37** : 1029, 1929.)

In an individual afflicted with Thomsen's disease there occurred at times, or daily, attacks of uncontrollable lethargy, deep and of long duration, out of which he could be aroused only with great effort.

Daily injections of 7-10 units of endo-pancreatic extract (insulin) caused this condition to disappear rapidly. Sleeplessness replaced the lethargy and the treatment had to be stopped.

Concerning the Endocrinology of and Therapy of Pathological Menstrual Hemorrhages in the Age of Development. — E. Glaesmer. (*Münch. med. Wochenschr.*, **76** : 406, 1929.)

It is a question of therapeutic experiment and result in a great series of menstrual anomalies in girls between 16 and 22 years who in the majority of cases exhibit "irritable hemorrhages" and in the preponderant number of cases a more or less marked genital hypoplasia.

A treatment of these irritable hemorrhages must *a priori* strive against an influencing of the follicular apparatus. The author attempted to exert this influence through cholin. Injections of cholin gave the same action in animal experiment as radioactive irradiation. Cholin is a constant constituent of many tissues. Owing to its blood-pressure lowering effect a hormonal property opposite to the adrenalin action is ascribed to it. The therapeutic experiences of the author are limited only to the field of the increased hemorrhages accompanying hypogenitalism at the age of development, and are favorable throughout. The results of the treatment were almost entirely good. In just as startling a manner, however, cholin acted on puerile hemorrhages resting on infantile basis. The most suitable preparation for cholin treatment proved to be borate of cholin. Cholin is superior to weak irradiation, since it requires neither expensive apparatus nor difficult technique and renders possible much more accurate dosage.

The Internal Secretions and the Problem of Rejuvenation (Experimental and Clinical Trial). — N. E. Ischlondski. (*Progrès méd.*, 44 : 767, May 4, 1929.)

The scientific study of the problem of rejuvenation is founded on the following biological conception: the genital glands send a specific hormone into the blood which circulating in the organism assures the development, then the preservation of the specific sexual constitution, one of the most characteristic pictures of youth. The most intimate relations exist between the genital glands and all the rest of the endocrine apparatus; the decrease or increase of internal secretion of the genital gland reflects on the activity of the other endocrine glands such as the pituitary, thyroid, etc. The aim of rejuvenation is reduced to stimulating the activity of the whole complex of the endocrine glands by the inoculation of an internal secretion, most frequently the sexual secretion. Without this intermediary stage, without the endocrine apparatus as a whole, there can be no question of a general rejuvenation. There are three stages to be distinguished in the story of the practical realization of the problem of rejuvenation. In the beginning we were limited to the transplantation of genital gland from a young animal to an old. The success of the operation in small mammals is unquestionable. In man this operation can not be executed for two reasons. (1) A practical impediment — the absence of human material

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for the transplantation. (2). A scientific consideration: the fate of each transplant depends on the regenerative capacity of the animal organism. This latter power is definitely manifested by lower animals and diminishes progressively in the more differentiated organisms.

In the face of the impossibility of transplantation of the sexual gland in man, the investigators have sought other means of action on the apparatus with internal secretion. Steinach himself tried to replace homoplastic transplantation of the gland by ligature of the canal deferens of the gland of the aged organism. Voronoff decided to use heteroplastic material (glands of anthropoid apes).

The author considers the results obtained by heteroplastic transplantation to be due to non-specific protein therapy. He arrives at the conclusion that the surgical method of rejuvenation viewed from the practical viewpoint at least at the present time, loses its importance. In his personal works on the application of the internal secretion of the genital glands the author made efforts to elaborate a chemico-biological method having as goal the extraction of the pure sexual hormone to be injected into the blood by parenteral route. A series of systematic works in the indicated direction has shown that a great quantity of the stimulating substances is found in the region of the hepatic tissue, embryonic tissue and placenta. Towards the end of the year 1924, the author was able to extract the genital incretion in its active form. Before undertaking the study of the action of the isolated internal secretion he had to elaborate an objective criterion to determine its action scientifically. The product given contains the active genital secretion only in the case where the introduction of this product into the organism realizes all the modifications in secondary sexual characters which Steinach was able to obtain by surgery. If this condition is not accomplished, the product can not claim the name endocrine.

The results of investigations on the rejuvenation of old, enfeebled animals were very encouraging. The experiences of the author prove not only that an effect of regeneration of the animal organism may be produced but also that the result obtained represents an actual rejuvenation, since it signifies a very distinct prolongation of life.

The author then began to systematically study the effect of the extract on man. Cases of senility in subjects from 60 to 82 years of age (32 cases); cases of psychic old age (4 cases); cases of precocious senility at the age of 34 to 50 years (31 cases); definite cases of weakness or complete arrest of sexual function in men aged 32 to 55 years (22 cases); cases of sexual insufficiency and hypo-development related to general asthenia in young girls (12 cases); cases of decrease of general metabolism and asthenia with varying etiology (11 cases); severe forms of anemia in the two sexes (18 cases). After treatment with the extract the patients showed an increase in strength and physical resistance.

One of the early signs of the action of the secretion was the restitution of normal sleep. In all patients a considerable increase of appetite was soon noted. There was increase of weight. A beneficial effect on constipation was also noted. In all cases where objective disorders of the blood were observed, these disturbances disappeared. There was a considerable increase in the number of red blood corpuscles. The action produced on sexual function enfeebled by age or prematurely was very remarkable. Even in cases of prolonged and resistant impotence treated unsuccessfully by various methods the author succeeded in raising considerably or restoring *in toto* the lost function. It is very important as characteristic of this action that after a treatment of short duration (12 injections) the action continues to increase and develop during long months after the treatment to become stabilized definitively. Relative to the restitution of the weakened or absent sexual function in women, most frequently in asthenic and underdeveloped young girls, 1 to 3 injections of feminine internal secretion suffice to cause a reappearance of menstruation. The author also mentions the beneficial action of the secretion in cases of disorders of the menopause: in cases of amenorrhea and dysmenorrhea. Quite an exceptional rôle may also be given to the action of the secretion on the psyche. An important rôle belonging to the second category of influences of the secretion on neuropsychic activity of the organism is also described: the action on memory, attention and capacity for concentration, the influence on the skin also presents considerable interest from the scientific as well as the practical viewpoint; it becomes more elastic as turgescence increases. During the experiments on ani-

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mals a considerable increase in resistance of the organism to infections due to the action of the secretion was noted. This was also observed in man.

The secretion does not act directly on the separate functions but regenerates the mechanisms of the organism itself: in the first place the internal secretory apparatus and the central nervous system. From the theoretical viewpoint this signifies that the fundamental principle of the influence does not present a substitution of substances lacking in the blood but rather a specific therapy of stimulation of activity of the endocrine glands.

The Action of Parathyroid Hormone on Tetania Parathyreopriva. — A. W. Elmer and M. Scheps. (*Klin. Wochenschr.*, 8 : 1407, 1929.)

On the basis of extensive researches the authors came to the following conclusions. Parathyroid hormone has a specific action on Tetania parathyreopriva.

The action of the parathyroid hormone surpasses by far that of other mediums. Treatment with parathyroid hormone by subcutaneous injection acts, within 5 to 15 hours in such a way as to quickly ameliorate the clinical evidences of tetany. In the worst tetany cases, where immediate aid is necessary intravenous injection of parathyroid simultaneous with the subcutaneous injection is required, which will bring apoplectiform recovery within 20 minutes to 1½ hours. The intestinal treatment with parathyroid hormone is also indicated in most of the more severe cases of tetany, especially in those in which other measures have failed.

Parallel with effecting amelioration of the clinical picture the parathyroid hormone influences the blood chemistry in that above all it intensifies the blood picture; it decreases the phosphorus and potassium. The influence of the alkali reserve and of the coagulation time is not constant.

The dosage of parathyroid hormone must be calculated individually and under the control of calcium content of the blood.

The duration of treatment with parathyroid hormone is varied. In acute cases with only transitory insufficiency it should only be administered during the existence of the clinical symptom; in most of the severe chronic cases it should be administered, similar to treatment with insulin, continually or with short pauses, and at best with simultaneous administration, *per os*, of calcium.

Evidences of a hypercalcemic syndrome were not constant.

The Properties of General Regeneration Hormones. — Fränkel. (*Arch. klin. Chir.*, clv, No. 2, 1929.)

In a first piece of work the author shows that the healing process after fracture of the femur presents a varied aspect in cases of bilateral fracture and particularly different when the fractures are not simultaneous. In a second essay Fraenkel showed that this variation reverts to two different hormones, to the plastic hormone and to the hormone of regeneration; their concentration in the blood varies even considering the state of tissue in regeneration. In this new work the author attempts to determine the action of the hormone. In his opinion the plastic hormone acts first for the development of new tissue and then prepares the tissue, through sensitization, for the action of the hormone of differentiation. Lastly it might have a threefold function: it stops the development of new tissue, at the same time it activates the differentiation and the destruction of these tissues. Its action on young regeneration tissue is insignificant, as on old tissue.

Observations on the Changes of Permeability by Means of Thyroxin. — A. Fröhlich and E. Zak.

The researches of these authors portend that permeability in March (tested in frogs bred in winter) is significantly poorer than in autumn (tested in frogs bred in summer). Treatment with theophyllin improves the poor permeability of winter frogs and in contrast decreases the better permeability of summer frogs for potassium iodide.

Further researches showed, for the case of potassium iodide, that, to a certain extent, the nervous system co-operates in the influence of theophyllin on the tissue, while the action of this diuretic in the case of grape sugar is without the participation of the nervous system. Now follows the researches of Cori, namely that the hyperexcitability of the sympathetic nerve in summer, which is indeed capable of overshadowing the effect of the simultaneously stimulated vagus, is dependent upon the thyroid gland which is active during the summer. It seemed of interest, therefore, to inquire whether, by the

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administration of thyroxin to winter frogs that had previously been treated with theophyllin, a modification would be induced that would be similar to that in summer frogs treated with theophyllin alone.

For this purpose edible winter frogs were preparatorily treated in March, 1929, with thyroxin. The animals remained under this process for about three weeks, they were treated in practically the same manner as those of March, 1927 and 1928, with exactly the same experimental procedure; four injections of 0.3 cc. Henning's thyroxin solution were given subcutaneously. These animals were then daily, in the usual manner, perfused with theophyllin and potassium iodide (Ringer solution containing 0.1 per cent potassium iodide).

The result of this experiment was that winter frogs previously treated with thyroxin plus theophyllin responded, in degree of permeability to potassium iodide, approximately the same as summer frogs treated with theophyllin alone; therefore it was possible the year round, to simulate the influence of the summer months in this respect.

Rectal Liver Therapy. — A. Hittmair. (*Deut. med. Wochenschr.*, lv, 398, 1929.)

In two cases of pernicious anemia that refused the oral administration of liver, a test was made by giving liver broth as an enema. In one case the test failed, the other case became profusely diarrhetic. In additional instances 300 gm. of liver from liver preparations, in suitable quantity was given daily in the form of suppositories. In some diarrhea again ensued, in some the test was satisfactory, but not so satisfactory as when liver was administered by mouth. In time the administration of small enemas with the addition of liver preparations will be tested.

Concerning the Relation between the Endocrine Glands and Abortion. — E. Imparato. (*Monde méd.*, xxxix, 793, 1929.)

It is not yet understood what is concerned in the recovery from abortion. The author offers a series of opinions of various authors and on the basis of his own observations he comes to the following conclusion.

From the literature and from his own experiments it can be concluded that abortion is allied with the insufficient activity of glands and that in the pathogenesis of this disease the ovary plays a significant part. It is true that in the treatment of the above mentioned disease with organotherapeutic products there have been both good results and failures, but with the limited knowledge we possess of the physiology and pathology of the internal gland secretions, one must be very cautious when he directs his attention to abortion or refutes it.

The Increase of Erythrocytes following a Secretin Injection Is Principally Traced Back to the Spleen. — F. W. Krzywanek. (*Pflügers Arch. ges. Physiol.*; ccxxii, 435, 1929.)

The influence of secretin solution from the dried small intestine (duodenum) of dogs was tested on normal dogs. In each case, at various intervals after the injection, a considerable definite increase in percentage of blood cells occurred, that varied between 22.5 and 34.5%. This finding coincides with the results of other authors; the explanation that this increase was a new formation or a thickening of the blood was refused for the reason that the factor in this case was the function of the spleen; for in animals with the spleen removed such a rise after secretin injection was not at all evident, or at least in only a very few cases.

Concerning the Biology of Placenta Extracts. — Gräfenberg. (*Zentr. Gynäkol.*, liii, 1795, 1929.)

Placenta extract derived according to the method of Coca showed in experiments with mice, a negative Allen-Doisy and a negative Zondek-Aschheim reaction. It was evident that the testicles of male animals treated with this extract were smaller than the testicles of untreated control animals. The extract effected no abortive action and did not respond in anaphylactic tests on guinea pigs, furthermore, no complement-building substance was derived in rabbits. In spite of these negative results in experimental animals the extracts were valid diagnostically in human beings. The albuminous extracts are a fine reagent. Skin tests on pregnant women often give a specific wheal picture, but a conjunctival reaction is not evident. One injection of the extract following hemorrhage intercepts pregnancy; however, an abortive action fails. The results with placenta extracts are favorable for the interruption of

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internal secretions. In its biological properties placenta extract shows noteworthy relations to allergic extract.

Folliculin in Amenorrhea. — Laffont and Chiapponi. (*Bull. Soc. Obstet. et Gynecol. Paris*, No. 6, 426, 1929.)

In a case of dysmenorrhea and amenorrhea a total recovery was obtained by treatment with folliculin. The doses administered were 60 units in 3 days. In another instance in which larger doses were given, the results obtained were not in accord with the others. Both instances demonstrate again that the influence of folliculin on menstruation is not yet comprehensible. Certainly the folliculin possesses an undoubted activity, but the ways and means of administration requires the proof of researches. Clinical observations and the results of research on the estrus in the laboratory must supplement each other.

The Value of Contractility of the Spleen Induced by Adrenalin in the Practical Clinic. — Jean Lerebouillet. (*Paris méd.*, xix, 79, 1929.)

V. Simone (*Minerva med.*, May, 1929) studied the applicability for clinical medicine of contractility of the spleen induced by the administration of adrenalin. Adrenalin gives satisfactory results in the diagnosis of latent malaria particularly in those forms in which the histological changes of the spleen have not yet brought about the contractility. In the treatment of malaria and the suprarenal insufficiency induced by it, it is profitable to combine adrenalin with quinine.

The adrenalin experiments can be adapted with caution in the diagnosis of cryptogenic septicemia, but only if the ejection of the microorganisms of the disease, stagnating in the spleen, do not threaten to become worse. In fact adrenalin can provoke the relapse to typhus and Malta fever or endocarditis lenta. Furthermore, one must always keep in mind the possibility of rupture of the spleen itself or of cysts or abscesses of the spleen, and hemorrhages which result from a violent expulsion of blood through the extension or constriction of the collateral veins, and instances of thrombosis of the splenic veins are also to be feared, therefore, adrenalin can only be used after great deliberation.

In therapy adrenalin can be applied to many cases of splenomegaly in which one has to consider a spleen tonus following the d turbance of the circulation; thereby a sort functional splenectomy can be attained certain diseases in which the hemorrha infarct of the spleen plays an important pa as is the case in many forms of hemol icterus. Lastly, by preliminary adrena injections by means of which the blood he in the spleen will be evacuated precauti will be had against the loss of a great quanti of blood in splenectomy.

Liver Therapy of Anemia in Nurslings and Young Children. — Jerachmiel Ligu (*Monatsschr. Kinderheilk.*, xliii, 513, 1929.)

The author treated twelve cases of anem of various sources in children with liver die In prematurely born children this thera induced an increase of hemoglobin from 62 74% and an increase of erythrocytes fro 2,930,000 to 4,400,000 resulted. It is possib to administer large doses of liver to olde nurslings much more readily than to the pre maturely born. In one instance, with pre maturely born treated with raw liver juice treatment had to be abandoned because thi stools resulted. Children in the first yea accept liver readily, however, in children tha have a distaste for it, liver therapy does no act favorably. In one case dyspepsia followe treatment and no result could be obtained In most children from 1-6 years good result were obtained with liver therapy and a increase of hemoglobin as well as erythrocyte resulted.

The action of the liver must evidently b founded in part on the iron content of the liver; more likely the profusion of vitamines in liver gives the significant results in trea ment. Liver contains all vitamines, especially Vitamine A, B and C, in large quantities. Herz in Hamburg agrees that good result were obtained in the treatment of anemia o children with the liver powder of Merck Dosage was commenced at 1 gm. of liver powder and was increased to 25 gm. Perhaps the technique with the nutrient medium wa be successful in affording good, easily digest ible preparations.

Clinical Diagnosis and Treatment of Pituitary Disturbance of Growth. — Lucke. (*Klin. Wochenschr.*, viii, 1476, 1929.)

The condition of primordial dwarfism, i which the individual is born abnormally small, is contrasted with the condition o

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pituitary dwarfism which exists when, in early childhood, in a previously normal individual, the function of the anterior lobe of the pituitary is impaired. In the ensuing disturbance of the growth process the bones show the first evidence. The development of the genitals remains stationary and involution does not take place. The state of the genitals accords with the other somatic development. True anterior lobe insufficiency shows itself in the arrest of development of normal intelligence in children. In very severe impairment pituitary cachexia occurs, an indication that, in older individuals, is the only evidence of the late appearing pituitary disturbance. The pituitary dwarf presents regularly an abnormal length of members with nether length and width in excess over the aggregate length. This state appears secondarily in the tardy development of the genitals. Fundamentally, the specific-dynamic albumin reaction and the blood sugar concentration are lowered. Often an eosinophilia is found in the blood. Changes in the sella turcica are seldom evident. As long as the ossification of the epiphysis has not taken place a year's treatment with substance from the anterior lobe of the pituitary can effect results, so that growth is noticeably improved and in females as further evidence of the efficacy of the therapy in an individual approaching puberty, the menses regularly ensue.

The Influence of Treatment with Spleen Extract on Lupus Vulgaris. — Artur Mahlo. (*Med. Welt*, iii, 971, 1929.)

On the basis of reports of Fliegel and Blayle concerning the healing of tuberculosis of the bone by the administration of raw spleen, the author treated three patients who had suffered for 15 to 19 years with lupus vulgaris, with spleen extract. Of this preparation of spleen (1 tablespoon is equivalent to 100 gm. fresh spleen) the patients were daily given 1 tablespoonful. Extensive improvement was evident locally as well as in respect to the general condition.

Concerning the Pathogenesis of Serious Conditions of Suprarenal Insufficiency. — G. Marañón. (*Presse méd.*, xxxvii, 1021, 1929.)

Among the instantaneous consequences of severe cases of the disease, the author mentions acidosis as a weighty one, if not the only one. Swingle stresses the fact that hypoglycemia and acidosis are both responsible, and the latter mainly is involved through inorganic sulphate and phosphate. Viale and Bruno rank among the factors the definite increase of blood viscosity (caused not by the loss of water but of plasma) and the radical conversion in lipoid metabolism. Likewise in all the worst forms of morbus Addisoni acidosis must be reckoned with before anything else, and therefore the author undertook treatment. He gave a diet rich in carbohydrates, followed by small insulin doses (5 units) with the addition of glucose (25 gm. in solution) three to four times a day, and next, alkali medication and caffeine.

Infantile Diabetes Treated for 5 Years with Insulin. — Mouriquand, Sedaillian and Mestrallet. (*Presse méd.*, xxxvii, 963, 1929.)

The authors present the case of a child who had lived in the hospital for 5 years and who, during this time, had been continually treated with insulin, in daily doses of 60-100 units. The child led a normal life and did not have a very strict diet regime. The urine eliminated amounted to 2-3 liters during 24 hours with a sugar content of 124.98 gm. and a blood sugar content of 5 gm. per liter. Its alkali reserve is good.

Concerning Intracardiac Injections of Adrenalin in Anesthetic Syncopes. — Perrin. (*Presse méd.*, xxxvii, 949, 1929.)

The author attempted the above mentioned method three times and concluded that as preliminary treatment it can be very efficacious. Everything must be ready in the operating room in order to give an intracardial adrenalin injection at a moment's notice.

Discussion:

P. Bertrand reported three cases of resuscitation of the heart with intracardial injection and Cotte reports of noticeable indirect results, so that he had to desist and he deemed it necessary to substitute another cardiac tonic with longer delayed activity. Chalier is skeptical concerning the above mentioned process, while Villard reports very successful results.

Rectal Treatment of Pernicious Anemia with Liver. — Hans Pulver. (*Therap. Gegenw.*, lxx, 294, 1929.)

In four cases of pernicious anemia very good results were obtained by the adminis-

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tration of liver through the rectum (hepatic powder with a liver value of 1:5 and 1:100). The compatibility for liver enemas and suppositories is on the whole good. Only in singular cases, in old people do complaints arise. Also in one patient the enema met with failure as it caused diarrhea and pains. A really successful liver therapy requires a very large amount of liver before a normal blood value is approximated or attained. Only then can one seek to preserve the remission with small quantities.

Further Researches on the Cardiac Hormone. The Action of the "Substances Actives." — R. Riegler and F. Tiemann. (*Pflügers Arch. ges. Physiol.*, ccxxii, 450, 1929.)

The authors could not corroborate the findings of Demoors and his collaborators who had reported that the "substances actives" derived from the Kieth-Flack nodes are the agents of automatism and as such are transmissible to the deficient or non-automatic activity of the heart parts, such as the isolated left auricle. The principle agent of the activity which was called "substances actives" is a non-specific substance existing throughout the organism, apparently belonging to the histamine group.

Experiments with the Problem of Pituitary Diabetes. — K. Velhagen. (*Klin. Wochenschr.*, viii, 1577, 1929.)

From the experiments of this author it follows that even with amounts of posterior pituitary hormone which have no physiological value, experimental evidence cannot be obtained that the blood sugar is a simple function of the proportion of the posterior pituitary hormone and insulin in the organism, and that it is not possible to induce a true case of diabetes by means of large doses of highly active posterior pituitary.

Concerning the Action of Kidney Extract on the Function of Contracted Kidney. — K. Stejskal. (*Klin. Wochenschr.*, viii, 1517, 1929.)

In seven cases of primary and secondary contraction of the kidney, decrease in blood pressure could be obtained by the intracutaneous injection of kidney extract and also of lipoid extract of the kidney. This action fails in genuine high blood pressure.

Discussion: E. Freund who obtained the extract added some general remarks to the report which culminated in the noteworthy complaint that students of internal medicine for the last ten years have had no interest in pathological chemistry.

L. Moszkowicz recalled the researches of Henschel in Basel, who with the aid of autolysates of various organs was able to create a specific action on the related tissue.

F. Necker was in doubt about the specific action.

E. Urbach reported on the intoxicating action of skin extracts.

On the Biology of the Placenta. — Rodekurt. (*Zentr. Gynäkol.*, liii, 1801, 1929.)

In two cases of hyperemesis a satisfactory result was obtained with treatment with placenta extract, in one instance a very marked success. Daily, 1-2 cc. was given intramuscularly (1 cc. equals 25 units). In three normal cases the influence of placenta extract was tested for the calcium and potassium content of the blood serum. The calcium content was always increased, in two cases likewise the potassium content. Folliculin to the amount of 8 units injected intravenously also gave after 6 hours a total calcium and potassium increase in the blood serum. Intracutaneous injection of this placenta extract as well as of total ovarian hormone, testifortan, thyroid gland oil, insulin, etc., gave no standard results.

Concerning Spleen Diet in Tuberculosis Patients. — P. Rüttgers and A. Kamsler. (*Beitr. Klin. Tuberc.*, lxxii, 1, 1929.)

The patients were given daily to eat 100 to 150 gm. spleen mostly in the raw state; the method chosen for administration was, for the most part, in the form of beefsteaks, lightly roasted on the outside and inside rare. In patients who did not tolerate this method of treatment doses of pulverized spleen extract (analogous to prepared liver extract) were administered. This diet was tested on 12 patients. Subjective improvement was evident in the greater number of cases. The temperature decreased, coughing and expectoration diminished. A falling off of the bacilli in the sputum was fairly constant. The often observed rise in hemoglobin content of the erythrocytes is important except that high mountain air had earlier induced a change

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in this respect. There was a favorable influence in the physical condition of the most severe cases also. The murmurs were drier; radiologically, the primary exudative foci showed progressively less productive character; in contrast, the cavities appeared the least influenced.

Constitutional Weaknesses of the Cardiovascular System in Young Children. II. — L. Doxiades. (*Ergebn. inn. Med. u. Kinderheilk.*, 35 : 98, 1929.) **Constitutional Weaknesses of the Cardiovascular System and Internal Secretion of Young Children. IV.** — (*Ibid.*, 140.)

Schittenhelm and Eisler have observed in healthy persons, after intravenous or *per os* administration of thyroxin a rise of respiratory metabolism and an acceleration of albumin metabolism. The blood undergoes a decrease in content of Ca : K. The hydrogen ion concentration experiences no characteristic change. In one patient in whom edema had occurred in the climacterium, total rapid disappearance of the skin symptoms followed treatment with thyroxin. The size of the heart was definitely reduced and the electrocardiogram was normal.

Relatively little is known concerning the fate of the thyroxin introduced into the organism. The oxidative processes increased by the thyroxin, above all, serve the reconstruction process in muscular activity (convalescence) in growth and development. Thyroxin serves the vegetative system and its action evidently lies in the regulation of the fixed equilibrium within the system. There is a report of earlier date concerning the action of thyroxin on the vessels of the heart. Thyroxin evidently produces a change in the permeability of the capillary endothelium, acting either directly from the blood or tissues, or indirectly, following the rise of the oxidative processes. In myxedema there is, evidently in consequence of the lack of thyroxin in the blood and tissues, a decrease of permeability of capillary walls with consecutive dilation of the venous ends of the capillaries, the venous subpapillary plexus and hyaline changes in the cells of the corium.

The author reports the case of a 9 year old girl with congenital athyrosis, who had been under observation since the 8th year. With the institution of thyroid gland therapy (thyroidin, 0.1, three times daily) in addition to improvement of the other disease symptoms, there occurred a favorable influence on the cardiovascular weakness. After 3 months of continuous treatment with thyroidin, the child showed splendid general condition. The consequent year of treatment with thyroid gland was successful in remedying the whole myxedema symptom. Today we trend away from treating myxedema operatively — through the transplantation of the thyroid. The oral administration of an organ preparation now is the best choice of method. The thyroid activity is regarded as specific, dependent upon the peculiarity of the iodin-albumin linkage in the substance. Exact dosage of the preparation is hardly possible. For chronic hormone treatment the author recommends the *per os* method; because of the possibility of appearance of additional symptoms, the intravenous method should be avoided in polyclinical patients. In mongolism thyroid gland treatment does not accomplish the same as in congenital myxedema.

Hydrops Articulorum. — O. Fellner. (*Med. Klin.*, xxv, 746, 1929.)

The author treated many patients who suffered from post-climacteric pains in the joints with placenta extract and good results were always registered. Preparations containing albumin were never utilized. In placenta therapy of hydrops articulorum intermittens it is certainly not a question of unspecific therapeutic effect, but rather one of hormone influence.

Concerning the Various Actions of Histamin and Adrenalin on the Blood Vessels in the Rabbit's Ear. — E. Flatow. (*Arch. exp. Path. u. Pharmakol.*, cxli, 161, 1929.)

Small quantities of adrenalin do not produce the same effect on the blood vessels in the rabbit's ear as similar treatment with histamin does. In intravenous injection adrenalin acts in opposition to histamin in concentrations which will contract the blood vessels in the rabbit's ear.

Circulatory Problems. — Frey. (*Med. Welt*, iii, 611, 1929.)

A hormone of the circulation is found in the urine and blood. The isolated hormone was injected intramuscularly into patients afflicted with angiospasm, twice daily, in small doses. The author presents a female patient who was quickly relieved of the angio-

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spastic symptoms in the hands, objective cyanosis, subjective tingling, after the injection. The hormone failed to elicit results only in a case of long-standing circulatory defect. In hypertonics the hormone treatment also achieved noticeable improvement, and progressive muscular atrophy was likewise favorably influenced by the injection of this new circulatory hormone.

Therapeutic Application of the Hormone of the Circulation. — E. K. Frey. (*Münch. med. Wochenschr.*, lxxvi, 814, 1929.)

The report of a female patient who had been successfully treated with injections of the hormone of the circulation. Relaxation of the angiospastic condition of the legs could be observed. In four patients with intermittent lameness a dose of 1/20 mg. for several weeks, given twice daily was sufficient to capacitate the patient. The action on hypertonics was good and in two cases of angina pectoris the coronary arteries were capable of being influenced.

Embolism and Thrombosis. — Fründ. (*Med. Welt*, iii, 610, 1929.)

Doses of thyroidin seem to have induced a suppression of post-operative thrombosis and embolism. The administration of thyroidin appears to be of real import and to have an influence on the composition of the blood and thence influences the coagulum. Reference was made to the rarity of thrombosis and embolism following goiter and Basedow operations.

Concerning the Relationship of Pituitary Gland and Hypothalamus to the Retention of Water. — E. Frank. (*Med. Klin.*, xxv, 679, 1929.)

The clinician who studies the action of substance from the posterior lobe of the pituitary gland in healthy persons and in those patients afflicted with retention of urine must come to the conclusion that there is involved here an incretion. The diuretic effect of the extract is not its natural capacity, but rather it enters if the pituitary substance is administered to narcotized animals or is introduced directly into the blood vessels. With the slow penetration after subcutaneous injection, there is always found in human beings and also in experimental animals, an inhibition of water diuresis. The powerful action of small quantities of pituitary substance on the retention of water in normal individuals is very evident in Vollhardt's water experiments.

If one administers at regular intervals, about every 3-4 hours, to patients suffering from diabetes insipidus, a subcutaneous injection of 1 cc. of an active extract, the patient is kept healthy as long as treatment lasts. The 24 hour urine output is immediately reduced from 10 L. to 1½ L. and under. Gorke observed in one case, on 3 test days, as much as 12 hours of anuria. The specific gravity of the urine rose extraordinarily.

Because of the knowledge that the substance from the tuber cinereum is an incretion carrier as well as an incretion storehouse, and that a vicarious, hypertrophic portion of the incretion organ is inseparably allied with it, the demonstrative force of the arguments presented in favor of the existence of an isolated center of water control and with it the experimental evidence that diabetes insipidus rests upon an affectation of the nervous element at the base of the mid-brain is destroyed; the true endocrine origin of the disease is well established.

Folliculin, Insulin and Diabetes. — F. Rathery and M. Rudolf. (*Bull. et mem. soc. med. hôp. Paris*, **44** : 741, 1928.)

The cessation of menorrhagic hemorrhages was observed following injection of folliculin in some cases. In two cases of severe diabetes in women a combined treatment with insulin and folliculin injections had as result a decrease of urinary sugar, disappearance of acetone and oxybutyric acid excretion. In one of the two patients the doubled folliculin dose had the opposite effect. In an 11 year old girl, who had not yet menstruated, glycemia was increased through the combined insulin-folliculin medication.

The Basal Metabolism. — P. Liebesny. (*Wien. med. Wochenschr.*, **78** : 1247, 1928.)

The clinical significance of the determination of basal metabolism is dependent upon the information obtained thereby concerning the function of the thyroid. B. R. Hill has shown that in 54 cases in which no typical symptoms of myxedema existed but only disturbances of circulation, the basal metabolism fell to about 13-47 per cent below normal. Thyroid therapy effected cure in 12 cases, improvement in 38 cases and left only 4 cases uninfluenced. Eppinger showed that in some

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cases of edema, which had remained refractory to every therapy, the administration of thyroid tablets proved to be the best diuretic. This by no means indifferent therapy will be resolved upon all the more readily in such cases when the determination of the basal metabolism gives strict indication for it. Eppinger also showed that individuals with normal kidneys present an accelerated chloride metabolism with the feeding of thyroid substance and finds moreover that patients with exophthalmic goiter show a rapid excretion of sodium chloride whereas myxedema patients retain sodium chloride. Through the determination of basal metabolism it can also be determined whether it is a question of an exogenous or endogenous obesity and when in addition the investigation of the specific dynamic albumin action is added, one can decide whether this obesity is dependent upon functional disturbances of the thyroid, pituitary or sex glands and thus hit upon the proper therapeutic measures.

Relations between the Digestive Tract and Blood Diseases. — Laqueur. (*Med. Welt*, 2 : 1538, 1928.)

In Holland good results were obtained in pernicious anemia by treatment with liver and liver extract prepared according to the instructions of the Committee for Pernicious Anemia (U. S. A.). Liver therapy is also to be tried in secondary anemias when other therapeutic measures remain without success. 1.0-1.5 gm. of the liver extract used corresponded to 100 gm. fresh liver. In most cases 3, 4 or 5 gm. of the liver extract suffice, but 12-15 gm. may also be given. The attempts at biological standardization of liver preparations have until now been without success.

The Internal Secretion of the Salivary Glands. — Goljanitzki. (*Ergebn. ges. Med.*, xiii, 125, 1929.)

In earlier experiments the author determined the following facts. Besides the production of secretion the salivary glands also have an endocrine function. The characteristic influence of the salivary gland incretion is on the condition of nutrition. In young animals the salivary glands have an important influence on the growth of the animal. Galeb-ski tested the problem of endocrine function of the parotid gland and found that the fluid derived from the parotid according to the method of Krawkow, is physiologically active, as is evident from the reaction on the blood vessels of the isolated rabbit ear and from tests on isolated rabbit and cat heart. On the isolated heart of these animals the fluid effects an inhibitory action for the most part. In five of six cases intravenous injection called forth a decrease in blood sugar that paralleled the amount of injected fluid.

These facts are evidence, therefore, that the parotid presents, besides an excretory function, a substance which acts on the individual organ as well as on the entire organism.

Endocrinology and Opotherapy. — G. Hallion and R. Gayet. (*Monde méd.*, xxxix, 411, 1929.)

From a general consideration of the administration of organ preparations in the clinic, the author reports, after mention of numerous contributions to the literature, concerning the administration of the following organ preparations: Liver, insulin, pituitary, suprarenal, thyroid gland, parathyroid gland and mammary gland. In an ensuing resume the diseases were enumerated in which organ preparations were administered with important or insignificant results. These are asthma, Basedow, cancer, diabetes, diphtheria, hemoptysis, cardiac neurosis, edema, insomnia and tuberculosis. For all these diseases the preparations used, the experiments and the results obtained were presented.

Skin and Venereal Diseases. — Max Joseph. (*Jahresk. ärztl. Fortbild.*, xx, 14, Skin Diseases, page 20, 1929.)

Pulvermacher presented the question whether the skin is an organ of internal secretion. Theoretically it is possible that the skin produces one of the parasympathetic tonic hormones and acts as a synergist with the suprarenal cortex, with which in this particular sense it is comparable.

Concerning the Rôle of Adrenalin, of Insulin and Glycogen Sugar on the Mechanism of Attacks of Angina Pectoris. — J. G. Katz. (*Fortschr. Med.*, xlvii, 303, 1929.)

Hetenyi worked with two cases of diabetes and cardiac sclerosis in which at the conclusion of every injection of insulin attacks of angina pectoris occurred, which were regularly excluded, however, if the patient

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received sugar simultaneously with the insulin. Strauss does not believe that direct injurious action of insulin takes place in the heart.

Chasanoff believes that the glucose contains a nutritive substance for the heart muscle. A series of experiments and clinical observations has shown that adrenalin and insulin are to be regarded as antagonists. The adrenalin circulating in the blood mobilizes the glycogen so as to transform it into glucose. Herter showed that intravenous injection of adrenalin induces glycosuria. Zuelzer determined that adrenalin glycosuria is excluded when insulin is administered simultaneously with the adrenalin. The chemical nature of insulin is not yet explained. Insulin acts not only on glucose, but also it incites changes in the metabolism of nitrogenous combinations, of fats and of lipoids. According to Krawkow, adrenalin distends the coronary arteries in the greater number of instances. Schwarzmann observed infallible antispastic activity of adrenalin in spastic condition of the heart. Some authors describe insulin as a vagotropic substance, others find a decrease in vagotonus and an abatement of spasmophilia through the use of insulin. Deicke reported on a case of angiospastic hemiplagia with motor aphasia, in which following the injection of 40 insulin units, hypoglycemic reaction occurred. The attack was renewed after two injections of 25 units, 6 hours after the second injection.

Concerning the Action of Post-Pituitary Extract on the Musculature of the Uterus. — Hermann Knaus. (*Zentr. Gynäkol.*, liii, 1162, 1929.)

The administration of pituitary extract to induce labor pains does not always produce the desired therapeutic effect. It is for example impossible, with the aid of pituitary extract to induce an abortion or to bring about premature birth. Therefore, it is quite inexplicable on what basis pituitary extract acts, for, before the normal termination of pregnancy, it can induce no labor symptoms or only impotent short ones.

Up to the present the explanation has been made that there is a weak sensibilization of the uterus for the activity of pituitary extract at this time of pregnancy. The processes which are concerned during all periods of pregnancy, during birth and the puerperium in the uterus, and which are significant for the reaction of pituitary extract can well be studied in the rabbit. In a well developed virgin animal, the tonus of the musculature of the uterus was markedly increased by pituitary extract. Intra partum, there occurs after the use of pituitary extract one of the most ideal forms of rhythmically increasing contractility for the progress of delivery. (Curves.) Because of this property to release uniformly flowing waves of contraction, pituitary extract is undoubtedly the best ecbolic. Twenty-four hours post partum the rabbit uterus is no longer capable of showing response to pituitary extract: the contractions analogous to those effected during the process of delivery. (Curve.) Forty days post partum a reaction similar to that of the infantile organ occurs after the use of pituitary extract. Depression of the muscular activity of the uterus is the base for the defective reaction to pituitary extract. Likewise the musculature of the uterus loses its power to react to extract of the post pituitary under the influence of corpus luteum.

Concerning the Influence of Administration of Thyroid Gland on Albumin and Fat Metabolism. — B. Kommerell. (*Biochem. Zeitschr.*, ccviii, 112, 1929.)

Two fasting experiments were undertaken on a dog in an interval of 5 weeks; during both fasting periods thyroid gland was fed. Representative of the action of feeding thyroid gland there occurred a basal metabolism rise of 30.5 per cent. This increased consumption of calories was defrayed on the average by 31.3 per cent albumin combustion and by 68.7 per cent fat combustion. The loss of body nitrogen during hunger, under thyroid gland activity reached almost double its original value.

The True Acidity in Isolated Portions of the Male Genital Apparatus of the Rat and Its Hormone Limitation. — Y. von Lanz. (*Pflügers Arch. ges. Physiol.*, ccxxii, 181, 1929.)

On the basis of his own observations the author determined that the true acidity in isolated portions of the male genital apparatus is not due to spermatogenesis, but rather to the existence of a generative gland substance in general. Bilateral castration differentiates the epithelium and determines the H-ion concentration of the secretion of this gland independently of the blood. The testicular

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hormone is active also after ligature of the ductuli efferentes. Apparently it was not absorbed in the epididymis.

Transplantation of Preserved Ovary. IV. Transplantation of Desiccated Ovary. — A. Lipschutz. (*Virchows Arch. path. Anat. u. Physiol.*, **272** : 245, 1929.)

Transplantation of totally desiccated ovary into the kidney of castrated male guinea pigs is always ineffective. By grafting ovary not completely desiccated, endocrine activity of the mammary gland apparatus occurs, which can become so intense that milk is formed. The endocrine action lies in a new formation of hormone in the grafted material in the organ of the host animal. Microscopic examination shows that the organ presents follicular development. The preceding damage to the organ does not inhibit the endocrine activity.

Investigations on the Origin of Creatin or Creatinin in the Animal Organism. — E. Abderhalden and S. Buadze. (*Zeitschr. ges. exp. Med.*, lxv, 1, 1929.)

As a result of the observations of various authors who, by the administration of thyroid gland substance induced evidences of creatin or creatinin, a test was made to determine whether the addition of thyroxin to muscle broth to which guanin had been added would influence the formation of creatin or creatinin. Hence it was evident that thyroid gland incretion caused the formation of creatinin and only without the addition of guanin.

Experimental Investigations on Corpus Luteum. — L. Brouha and H. Simonnet. (*Presse méd.*, xxxvii, 591, 1929.)

Corpus luteum extract, injected into normal female rats causes the suppression of the estrous cycle, provided the dosage is large enough. The genital tract assumes an appearance similar to that observed in castrated animals. With smaller doses a condition is established suggestive of a pseudo-abortion, without the characteristic estrus, but with the development of the uterus. With weak doses extention of the period of estrus only is obtained. In sexually immature animals the extract preserves the first estrus. In castrated animals no development occurs either in the uterus or in the sex glands. The extracts act on the estrous phenomena evidently in such a manner as to suppress the production of folliculin, but not its activity, for if folliculin and corpus luteum extracts are simultaneously injected the latter does not prevent the action of folliculin.

Hormone of the Anterior Lobe of Pituitary as Related to the Male Genital Tract. — L. Brouha and H. Simmonet. (*Presse méd.*, xxxvii, 591, 1929.)

Daily intramuscular implantation of portions of the anterior lobe of the pituitary show that this gland exercises a remarkable stimulating action on the male genital tract (rat, mouse). The activity of the anterior pituitary extract varies with the method of preparation and often with the dose administered. If the active principle which is contained in the urine of women at the beginning of pregnancy is used, there may be regularly observed a striking change in the genital tract of sexually immature animals, similar to that in adults. With extract of anterior pituitary prepared by alkaline method a definite development is obtained when small doses are employed and in contrast, an intensification or a retrogression with larger doses. We do not yet know whether this activity is referable to two antagonistic substances, or to a single substance which is active variously when injected.

The Zondek-Aschheim Pregnancy Reaction. — R. Brühl. (*Deut. med. Wochenschr.*, lv, 696, 1929.)

1. A positive result with the pregnancy reaction of Aschheim and Zondek gives very definite evidence of pregnancy. The negative result of the reaction excludes pregnancy with 100 per cent surety.

2. It is very evident that in the anterior lobe of the pituitary gland at least two hormones are formed. The one effects maturation of the follicles and is found usually in the urine of climacteric and castrated females, the other influences the formation of corpus luteum and is especially evident in pregnancy.

3. The hormone could not be demonstrated in the urine of mares in foal or cows with calf.

Organ Extracts in Their Action on Immuno-Biological Processes. — Pockels. (*Münch. med. Wochenschr.*, **76** : 770, 1929.)

Animals difficult to immunize were made good producers of antibodies by the injection

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of spleen extract. Spleen and lung extracts were administered orally to human beings in order to determine the active di-immunization. A specific influence was derived.

Insulin and Nutrition Depots. — A. Löw and A. Krčma. (*Biochem. Zeitschr.*, **206** : 360, 1929.)

The author studied the problem of how insulin, administered under various conditions affects the carbohydrate capacity of fat. The mouse served as the experimental animal.

The experiments show that a marked lessening of liver carbohydrate is induced after insulin injection. The beginning of the decrease can be determined 1½ hours after the injection. The decrease in liver glycogen is to be accounted as a direct action of insulin. In fatty tissue only inconsequential changes of carbohydrate content could be observed. The contrast with the action on liver tissue is important. It proves that insulin acts differently on fatty tissue as compared with the liver. The observations made at that time, namely that in fasting rats, more glycogen was found in the fatty tissue than in normal animals, permits the conclusion that carbohydrate can also be formed in the fatty tissue. The experiments of the author make it evident that the lobule organ can claim this function.

Concerning the Treatment of Milk Retention. — Walter Mestitz. (*Münch. med. Wochenschr.*, **76** : 782, 1921.)

The painful retention of milk, especially in sensitive women, must be actively combated. In this case diuretics are useful. Because thyroidin is a good diuretic, Kraul gave thyroid gland substance as treatment for milk retention and obtained good results.

Cell Formers and Cell Forms of the Blood. I. Changes in the Blood Formers during Complete Cure of a Granulocytosis. — W. Stockinger. (*Zeitschr. ges. exp. Med.*, **65** : 27, 1929.)

The author was able to determine that in granulocytosis, adrenalin acted to cause an increase of cells in the blood. The less this is, the worse off the general condition of defense in the organism. The cell increase after adrenalin is effected by the entrance of large unformed cell elements into the blood circulation.

Further Investigations on the Relationship between the Pituitary and the Ovum with Its Accessory Glands. — Hermann Siegmund. (*Münch. med. Wochenschr.*, **76** : 776, 1929.)

Following the implantation of rather large amounts of anterior pituitary tissue into infantile female mice, there appeared evidences of premature estrus due to the premature mobilization of hormone incretion in the ovary. After the implantation corresponding to high dosage it is even possible in the pregnant mouse to arouse the latent follicle of the ovary in pregnant state and cause proliferation and luteinization of the follicle cells. However, it is not possible to demonstrate estrus symptoms in the vagina during pregnancy neither could the ovary be forced experimentally to further incretion by the administration of anterior pituitary incretion. The release of the excretory function of the ovary, *i. e.*, the evacuation of ripe ova, could not be ascertained by the author. The researches performed according to various physiological methods all speak for the inhibition of each ovulation during the time of function of the corpora lutea. The author reports that the pregnancy test of Aschheim is exclusively reliable. Many contributions deny the control of the sexual function by the pituitary; the more prevalent perception that the ovum and its accessory glands have an active effect on the expiration of sexual function must be correct.

Hydrops Articulorum Intermittens. — H. Schlesinger. (*Med. Klin.*, **25** : 746, 1929.)

Many authors report that the therapeutic reaction in hydrops articulorum intermittens is unimportant. As may be seen from the literature, the disease is associated with the function of the female genitals. It occurs after prolonged puberty or after lactation in an abortion or parturition. The author applied therapeutics to this etiological association, and treated the patient described with placenta extract, throughout 5 months one injection every second day. The swelling was lessened, it did not last very long and it was no longer painful. The interval between attacks, which formerly was 8 days long, now was 12 days. The author believes that still better therapeutic effects may be obtained by the administration of stronger extracts — those given were quite weak.

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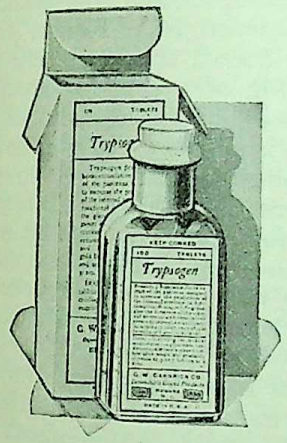
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Text Book Opinion

"The opposers of the oral method must remember that it will not produce the immediate and dramatic result that injection produces but then it does not expose the patient to the dangers of hypoglycaemic reactions nor the increasing dread of the needle."

(W. M. Crofton, *An Outline of Endocrinology*, 1929.)

In actual clinical use Dr. Crofton found Trypsogen "to work very well".



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Test of Insulin-Induced Hyper-Hypoglycemia in Normal Subjects and in Pathological Syndromes (Emaciation, Obesity, Diabetes). — F. Moutier and L. Camus. (*Arch. mal. app. dig. et mal. nutrit.*, **19** : 297, 1929.)

The matter taken up in this article concerns a combination of a hyperglycemic and a hypoglycemic process an assumption depending on the hypoglycemic reaction of one person. However, one can not draw unconditional conclusions from work on emaciated individuals; indeed several of the thin persons observed by the author reacted strongly to the insulin test and presented quite variable results when insulin was given in therapeutic feeding. In any case it is determined that the test never did the thin people any harm. Hypoglycemic symptoms occurred only in persons with intense bulimia. Patients with dysthyreosis and some with sympathicotonic symptoms reacted quite easily. The test is also valuable for the comparison of the activity of insulin preparations of various origin.

Contributions to the Study of the Importance of Blood Glands for the Digestive Tract. The Action of Adrenalin and Insulin on the Secretion of the Succus Entericus. — B. A. Schazillo. (*Arch. Verdauungskrankh.*, **45** : 264, 1929.)

It has long been known by the clinician that the patient with hypothyrosis suffers from obstipation and the patient with hyperthyrosis suffers from diarrhea. Marbé, after feeding dogs with thyroid gland, observed a rise of intestinal secretion. The study of the action of adrenalin and insulin on the secretory function of the intestine has not only a theoretical interest, but also a great practical interest. The author undertook investigations on this problem, and found:

1. That the irritating action of subcutaneous injection of adrenalin — particularly at the height of digestion — is not favorable to digestion after meat extracts have been consumed. One gains the impression, therefore, that in this case the irritation is caused by an irritating substance produced by the intravenous injection of the incretion medium. Adrenalin in subcutaneous injection increases the activity of the sympathetic nerve element in the organs. At the culmination of digestion, however, the same quantity

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of adrenalin can increase the irritating effect on the animal only when given intravenously.

2. The irritating action of small doses of insulin on dogs is elucidated; on the basis of the investigation, it is to be assumed that the secretory process of the intestine was influenced both by adrenalin and by insulin. Insulin arouses the intestinal secretion in fasting dogs as well as at the culmination of digestion.

Influence of Internal Secretion on Dermographism. — G. P. Sanna. (*Med. Welt*, **3** : 530, 1929.)

The author has studied the variation in color, the time of appearance and the duration of dermographism in persons to whom had been given a high dosage of various internal secretion substances. Thyroid gland, suprarenal, pituitary, testicular and ovarian substance were administered *per os*. One hundred individuals were tested, of whom twenty served as controls.

Ovarian preparations (extract of the generative glands of lower vertebrates) brought out red, superficial dermographism with significant lessening of time of appearance and disappearance as well as the entire duration of the symptom itself. Besides the reaction was very intense: reflex dermographism.

Male generative glands (testicular extract of lower vertebrates) gave almost the same symptoms.

Thyroid gland preparations called forth a very pronounced, superficial, red dermographism, often accompanied with lateral white streaks, with definite lengthening of the time of onset and disappearance of the symptoms and great increase in the duration. The degree of severity was somewhat diminished.

The same symptoms were called forth by entire suprarenal extract, but the reaction was stronger, and more easily provoked.

With pituitary extract no definite action on dermographism was obtained.

The Functional Significance of Isolated Portions of Pituitary Gland. — A. Biedl. (*Endokrinologie*, iii, 241, 1929.)

On the basis of numerous observations it is now a well known fact that the anterior lobe of the pituitary contains a hormone capable of effecting the maturation of the sex glands. With consideration of the information that, in mice, the administration of large quantities of anterior pituitary hormone causes complete luteinization of the ova... overdosage in the form of a single large app... cation of mouse units rather than long-co... tinued parenteral application of anter... pituitary hormone is to be guarded again... Whether the anterior lobe incretion te... any relation to the carbohydrate metaboli... incidentally has not yet been determined i... this instance.

The pars intermedia of the pituitary wit... the help of its incretion influences the requir... ment and consumption of substances, th... general variations, the constancy of bod... heat, as well as the activity of isolated vegeta... tive organs. The extensive informatio... which we have gathered concerning the acti... of the extracts of the pars intermedia and posterior lobe gives evidence of the metabol... action of these parts of the pituitary. Th... question of where this active substance orig... nates is not argued, nor is its hormonal natur... generally acknowledged. Kamm and hi... colleague have shown that in pituitrin there is not a question of a single substance, bu... rather of several substances. The substances possessing either promoting or inhibiting activity on diuresis, according to existing conditions, seem to be contained in the frac... tion with pressor activity. The fat metaboli... ism was influenced in such a way that after administration of pituitrin there occurred a considerable falling off of fat in the blood and a lessening of the ketone bodies.

The pituitary incretion acting on the center of vegetative metabolism can interfere indirectly in the function of the animal nervous system.

The pars nervosa and the adjoining stalk were found to have no incretory significance.

The functional significance of the pars tuberalis is not explained.

Endocrine Disturbances in Childhood. — Rudolf Neurath. (*Wien. klin. Wochenschr.*, **42** : 617, 1929.)

In the last stages of embryo life and soon after birth a definite overweight of the sex glands and cortex of the suprarenals occurs... that is evident in the anatomical size and i... the quality of the skin and hair. Besides th... intensified growth of the sex glands an increase in metabolism, due to unusual increase in... hyperactivity of the thyroid gland, is charac... teristic for puberty; growth in height at this period is fostered by the anterior lobe of the pituitary. In adolescence the se...

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glands attain prominence; metabolism is undertaken by the hormone of the thyroid gland and the adrenal system and the lobule apparatus of the pancreas become more and more important for consumption and metabolism. Congenital thyroid gland defect is evident in the characteristic symptom of myxedema. In children this form is developed soon after birth.

There are also constitutionally hypothyroid individuals who have great need for hormone or whose thyroid gland functional capacity is greatly lowered — torpid adipose persons with lowered basal metabolism.

Also the temporary hyperthyroidism producing obstipation in newborn infants, which is always associated with the obstipation of the nursing mother, must be mentioned. The treatment of sluggishness of the bowels in both mother and child is promptly effected by thyroidin. In no phase of endocrine disease has substitution therapy acted so extraordinarily and showed its efficacy as in the treatment of hypothyroidism and athyrosis. Substitution therapy is accomplished by the ever increasing improvement of production of the hormone of the thyroid gland. As a daily dosage for nurslings thyroidin was given in tablet form of 0.1 gm., older children were given as much as 0.3 gm. The action of the hormone on the physical symptoms as well as on the psychic deficiencies is important. The endocrine function of the suprarenals is twofold. Recently, E. Schwarz performed investigations from the viewpoint of modern embryological opinions to shed light on the problem of interrenalism. In order to bring out all the evidences of interrenal syndrome depending on suprarenal hypertrophy, we have only to admit that the excessive activity of the suprarenals on the sex-determining gene complex of the chromosomes is such that the factor bound to the X-chromosome is impaired either by its own mitigation or by that of its opposing medium. Accordingly, the zygotic sex-determination is capable of being influenced by hormones.

Method of Increasing and Decreasing Secretion of Milk at Parturition. — Michael Wachtel. (*Zentr. Gynäkol.*, **53** : 987, 1929.)

The attempt to cut off as quickly as possible an existing milk secretion, or not to "allow" the milk secretion to occur, is important in cases of intrauterine death of the fetus; further in women who have suffered a miscarriage in the later months of pregnancy, or whose offspring has died soon after birth. The congestion and tension of the breast full of milk is very painful to women. The treatment of this uncomfortable condition is most easily and simply effected by thyroidin. The earlier torment inflicted, of having the women go thirsty or to stem the function of the mammary glands by purgatives has become superfluous. After the administration of thyroidin, besides greater permeability of the tissues and influence on the osmotic oncotic pressure, there occurs a dispergence of the white blood corpuscles, for the increase of albumin and the decrease of globulin and fibrin. The result, therefore (Starlinger) is a much augmented capacity for swelling and a greater power to take up water. Kraul mentions the fact that he gave this thyroid gland preparation too, in painful condition of the breast during menses and obtained results. The author reports on twenty women to whom he gave early in the day and in the evening, 1 thyroidin tablet 0.3 and at midday he supplemented this treatment with 1 tablet of diuretin 0.5 gr. The treatment was continued for 3 days. Milk secretion did not occur at all. No harmful consequences have ever occurred.

Communications on the Activation of Adrenalin by Thyroxin. — T. Zimmermann. (*Biochem. Zeitschr.*, **206** : 369, 1929.)

The author undertook investigations to determine whether the activity of adrenalin could be influenced by the secretion of the thyroid gland. Following this the decrease of the glycogen content of the musculature after adrenalin injection was determined, and then the action of similar doses of adrenalin was noted after a thyroxin injection had been made. From all these tests it was learned how variable is the action of adrenalin. After adrenalin 1:10,000 there was a decrease of 21.8 per cent; with adrenalin 1:1000 this was found to be 25.28 per cent. The glycogen content of the liver with adrenalin 1:10,000 amounted to 1.79 per cent (resp. 2.16 per cent) with adrenalin 1:1000, 0.90 per cent.

If adrenalin injection is made 6 hours after a thyroxin injection, the diminution of glycogen in the muscle amounts to 37.6 per cent, the liver glycogen dropped to 0.257 per cent. Hence upon consideration of the

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thyroxin alone it follows that the thyroxin increases the activity of adrenalin for carbohydrate metabolism.

A Case of Cryptogenic Pernicious Anemia Which Proved Refractory to Simple As Well As Combined Liver Therapy.—Emile Weil. (*Paris Med.*, **19** : 416, 1929.)

Report on a case of cryptogenic pernicious anemia diagnosed as such clinically as well as by post-mortem examination. The patient, who had shown a remarkable improvement throughout a month of combined liver and insulin therapy, a few weeks later suffered a relapse and became entirely refractory in this stage to liver-insulin therapy. The author emphasizes the fact that too little observation has been made on those cases resistant to liver therapy, and he was supported in this opinion by Fiessinger and Tixier.

Severe Hemorrhage after Delivery. Non-Operative Treatment. Cure.—Voron and Pigeaud. (*Bull. Soc. obstet. et gynecol. Paris*, No. 3 : 225, 1929.)

In a 21 year old primipara, 2 days after spontaneous delivery, there occurred rise in temperature with chills and on the 10th day severe hemorrhage, which ultimately assumed a menacing aspect and made remedial measures necessary. The patient received only ergotin injections. Then, because the pulse became worse and further, anemic symptoms appeared, the patient was given injections of pituitary besides the ergotin injections, whereupon the hemorrhage was at once diminished, despite the noxa of a transport for eventual hysterectomy, and was entirely stopped within 23 hours by repeated pituitrin-ergotin injections.

Concerning the Relationship between Psoriasis and Ovarian Function. — E. Vogt. (*Monatsschr. Geburtsh. u. Gynäkol.*, **31** : 385, 1929.)

The hormonal theory always plays an important rôle in the explanation of psoriasis. Since the theory of purely thymogenic origin is so disputed, it might appear that the thymus gland plays a part in conjunction with the sex glands. The author reports on four cases in which the relation between the origin of the skin disease and the activity of the female sex glands seems quite certain. Case 1 gave evidences three times of this skin disease which first appeared in the 12th year, before the beginning of the menses (which beg in the 14th year); the second time, after birth of the first child, when amenorrhea lactation was present; the third time, after the commencement of the menopa In the second case psoriasis occurred in course of amenorrhea of lactation; in third case, after roentgen amenorrhea in 50 year old female patient; in the fourth ca after operation, radically, of a myoma. B observed that the disease appeared after the physiological amenorrhea of pregnancy Scheuer observed a pronounced aggravation the symptoms during pregnancy. Practical hormone substitution therapy with ovari preparations is to be recommended in the treatment of psoriasis, the most protracted and severest of those diseases requiring trea ment; it may be recommended all the mo since effective, active ovarian preparation can now be prescribed, to be taken n only parenterally but also orally. Further may be noted that psoriasis has been treated repeatedly with insulin and good result ensued. From this one can assume a pure endocrine action of the pancreas hormone However, there can also be the matter of a vitamin effect, the insulin working as a vitamin agent. Indeed the pancreas hormone contains abundant amounts of vitamin D.

Concerning the International Standardization of Drugs. — L. E. Knaffl. (*Wien. klin. Wochenschr.*, **41** : 1495, 1928.)

The Hygiene Organization of the League of Nations has suggested all the methods of standardization of drugs, also such as can be standardized by biological method. As regards pituitary extract, the Conference is of the opinion that the desiccated preparation of the posterior lobe of fresh pituitary prepared by acetone extraction, which has been proposed by Prof. Voegtlin at the Edinburgh Conference, is suitable to be accepted as international standard preparation. For the biological standardization of the oxytocic activity the test on the isolated uterus of the virginal guinea pig according to the Pharmacopoeia of the United States, 10th Edition is recommended.

For the estimation of the action on the blood pressure comparative investigations on anesthetized dogs or on decapitated cats are recommended. For the determination of the antidiuretic action the test on the unanesthetized dog, on the healthy human being or

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on patients with diabetes insipidus is regarded as suitable. The Commission is of the opinion that in the event of the antidiuretic action being due to a third substance, there is the possibility of expressing the activity in antidiuretic units of the same standard powder. Still further investigations are, however, necessary to establish the unity and strength of the standard preparations of the different firms with respect to their antidiuretic action. In all cases a unit should be that which corresponds to the action of 0.5 mg. of the standard powder.

As international standard preparation for insulin, the desiccated preparation of hydrochlorated insulin is recommended, which was established by a resolution of the Edinburgh Conference of the Medical Research Council of Great Britain. One mg. of this standard corresponds to 8 such insulin units (1 unit — 0.125 mg.) as were previously defined by the Insulin Committee of Toronto University. The appointment of a sub-committee is recommended which will submit proposals with regard to the permissible organic desiccated residue per unit and with regard to the testing of the strength.

With respect to thyroid preparations the Genoese Conference was of the opinion that the biological estimation of thyroid substance was not in general necessary, but the iodin content in specific union with the active substance can be considered as measure for the therapeutic value. In order to recognize any increase of artificial iodin content, for example with iodides, the estimation by the so-called acetonitril method (Reid Hunt and Straub) is proposed. As comparative standard for the biological testing a desiccated preparation from healthy thyroid with an iodin content of 0.2 per cent is recommended.



DYSMENORRHEA

A HOSPITAL REPORT

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Leiner's Dermatitis. — Szentléleky-Szász. (*Monatsschr. Kinderheilk.*, **40** : 362, 1928.)

In nurslings with exudative diathesis and in those who suffer from Leiner's dermatitis subcutaneous injection of ½ to 1 cc. posterior pituitary extract caused the skin to become very pale within a few seconds and the skin process often disappeared after 24 hours; at the latest, however, within 4 to 5 days. The more severe the skin changes the more intensive the pallor. In one case of Leiner's dermatitis, under the action of posterior pituitary extract, the liver swelling decreased in striking manner.

Better results were obtained with decrease of the dose. The more severe the process, the smaller the dosage; on the average 1/3 cc. twice daily, in all 4 to 5 injections. The edema which lasted for a long time with 1 cc., did not come into question with small doses. In severe eczema also favorable results were obtained with post-pituitary extract. J. Pilcher (Cleveland) gives subcutaneously or intramuscularly in eczema 1‰ extract of suprarenal to 0.1 to 0.3 cc., and obtains cessation of the itching.

Concerning the Question of the Decrease or Abolition of Labor Pains. — Hoehne. (*Zentr. Gynäkol.*, **52** : 2773, 1928.)

The slight degree of narcosis intoxication with ether or ethyl-chloride injures — in otherwise excellent execution — the activity of the labor pains on the bearing down process. For this reason the simultaneous intravenous injection of a pituitary preparation is important in such cases, and the substitution of Kristel's extraction for the lacking abdominal muscular pressure.

Insulin, Synthalin and Glukhorment. A Comparative Investigation concerning Their Action on Glucose Fixation through Cells. — E. B. Salen and T. Nyren. (*Acta med. scand.*, **69** : 69, 1928.)

Experiments with synthalin and glukhorment carried out under corresponding experimental conditions show an effect of increasing fixation of glucose for both these substances identical qualitatively with that of insulin. Under the supposition that glukhorment contains a substance identical with synthalin or closely related to it chemically, the assumption is justified that the effect of increasing glucose fixation observed is wholly conditioned through a synthalin-like substance present in the glukhorment. The experimental results of the authors support the opinion that the glucose fixation-increasing action of insulin is a specific insulin effect which also has an essential significance for the function of insulin *in vivo* (for its sugar-regulating function). The latest attempts to define insulin chemically (Abel and his associates) have led to results which speak rather for than against the assumption that the specifically active constituent of insulin can be a substance closely related to synthalin. The demonstration of a qualitatively identical action *in vitro* of all three substances is calculated to support still further the whole conception.

A Chemical Reaction to Vitamins and Hormones. — E. Christensen. (*Münch. med. Wochenschr.*, **75** : 1883, 1928.)

The extensive harmony between vitamins and hormones pointed out by E. Vogt, suggested the question whether hormones give the same color reaction as is obtained when vitamin-containing extracts are diluted with phosphoric pentoxide. Accordingly, preparations of ovary and testis were tested and in both the same reactions with phosphoric pentoxide were determined. Moreover, a large number of commercial insulin preparations were examined and it was found that all without exception gave a positive phosphoric pentoxide reaction, to be sure in very different strengths, which seems especially noteworthy. There came to light, therefore, with respect to the reactivity to phosphoric pentoxide, various differences between the individual brands of insulin, such as were earlier described concerning the albumin content. To what extent these differences parallel the therapeutic usefulness of the individual preparations must first be explained by further investigations.

Hypergenitalism and Macrogenitosomia. — Serdukoff. (*Rev. franç. endocrinol.*, **6** : 378, Oct., 1928.)

By hypergenitalism is meant the precocious appearance of puberty with the organism remaining in a state of infantile development. Cases of hypergenitalism are much less frequent than the various forms of insufficient development and hypofunction of the genital organs. In definite clinical cases the symptomatology of hypergenitalism or macrogenitosomia in women presents a

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complex of primary or secondary symptoms translating the abnormal precocious development and premature manifestation of the functions of the genital glands. Almost always following precocious development of the genital organs, there occurs an exaggerated development of the whole body, muscles and skeleton. In relation to this exaggerated development, at the beginning, the attention is drawn by the tall stature and by a considerable weight.

Finally as the affection develops there is precocious ossification of the epiphyseal zones and the tendency to growth stops. The height, in general, in cases of hypergenitalism does not reach dimensions such as are observed in gigantism.

Hypergenitalism or macrogenitosomia is of endocrine origin. The height of girls suffering with macrogenitosomia exceeds by a third or a fifth that of their comrades; their weight may be double the normal. From the constitutional point of view one does not always find congenital factors of functional anomalies of the genital glands. Frequently girls suffering from this disease come from fertile families (nine, twelve and fifteen children) with twins and even triplets. The precocious appearance of menstruation is also found. At times familial hypergenitalism is observed.

The tendency to increase in size in the course of macrogenitosomia is also manifested for certain secondary sex characteristics: mammary glands, development of hair, development of external genital organs. In addition to the morphological modifications of the genital organs the precocious appearance of menstruation is observed.

The syndrome of genital hyperfunction in both sexes is manifested in childhood and assumes the character of pathological manifestation of hyperfunction of the genital glands: Hyperovarianism in women and hyperorchism in men. Among the characteristic symptoms in males there must be cited an abnormal increase in height, the precocious appearance of pubic and axillary hair, and the enlargement of the genital organs; the psychological changes and voice changes; sexual desire appears prematurely.

Etiology and pathology show that hypergenitalism or macrogenitosomia represents a disorder of endocrine equilibrium. The literature shows that cases of macrogenitosomia may have a primary character, that is, when there are morphological modifications in the genital glands themselves; the secondary forms of macrogenitosomia are related to affections of the pineal gland and suprarenal cortex.

In the cases of primary ovarian macrogenitosomia the presence of such ovarian tumors as adenocarcinoma, folliculoma and sarcoma is most frequently encountered. In the secondary forms, an important position is occupied by the affections due to pathological states of the pineal gland. Most frequently, such an etiology is related to the destruction of the pineal by tumors (teratomas, gummas, tuberculomas, hydrocephalus). In such cases of destruction of the pineal gland, the latter is unable to restrain the appearance of genital manifestations.

Moreover, as frequent cause of precocious puberty, tumors of the suprarenals must be considered: these tumors are most frequently hypernephromas, from the morphological viewpoint, which implies the increase in function of the cortical substance. The suprarenal cortex, according to its functional role, presents a synergistic action with the genital glands. That is why it is natural that increase in the intensity of the functions of the cortex substance of the suprarenals should produce a stimulating action on the development and growth of the genital organs and also contribute to the development of the secondary signs and growth of hair.

Hypergenitalism is not always a monoglandular endocrinopathy (affection of the ovary, of the pineal or of the suprarenal) and cases have been described in which simultaneous lesions of the ovaries and suprarenals have been observed. In these complex cases of hypergenitalism, symptoms of Addison's disease were present. In the cases where the macrogenitosomia bears the character of polyglandular etiology, obesity may be added to the precocious increase in height and to the development of the secondary sex characteristics.

In certain typical cases, in the presence of a monoglandular endocrinopathy, the diagnosis does not present special difficulties. In other numerous cases, in the presence of a polyglandular etiology, the diagnosis may be difficult. On the one hand, it is difficult to discover the participation of the affected glands and, on the other, it is not always easy to differentiate hypergenitalism from gigantism. The examination of the epiphyseal zones may establish the boundaries of the

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hypergenitalism and the gigantism; at times radiography decides the question one way or the other. In gigantism, the epiphyseal zones remain ununited for a long time; whereas in hypergenitalism, with precocious puberty, the arrest of growth in height takes place towards the age of 8 or 10 years.

In complicated cases, to discover the etiology and differential diagnosis, the reaction of Luttge and Mertz may be used.

Prognosis is intimately related to the etiology and the degree of specific involvement of the endocrine glands. Certain slight cases may be regarded as a manifestation of an almost physiological hyperovarianism following which precocious puberty supervenes and a regular menstrual function. The prognosis becomes more complicated in the cases where following the appearance of precocious menstruation in children, a prolonged loss of blood occurs whose real cause is malignant degeneration of the ovaries: their total ablation does not always suffice to prevent malignant recurrences in other organs.

Where hypergenitalism is intimately related to infectious, syphilitic, tuberculous processes, specific treatment may give a positive symptomatic effect as far as cessation of the menstruation is concerned and regulation of the endocrine equilibrium. At times the regression of all the signs of precocious puberty is observed. Such a result is at times possible in the rare cases where the hypergenitalism has developed following a neoplasm of the genital glands, which has been subjected to radical ablation of the affected glands.

Treatment, according to the case, is directly related to the importance and character of the lesion of one or the other gland dominating this endocrinopathy. In the greatest number of the cases where a malignant affection of the pineal or suprarenals is involved, it is impossible to obtain cure. In certain cases, satisfactory results may be obtained with applicatior of roentgen therapy to the ovarian region.

Organotherapy gives an inconstant symptomatic result, although adrenalin is sometimes capable of arresting the flow of blood in precocious menstruation. Serotherapy by the serum of castrates does not give appreciable result in the cases of considerable hemorrhages. In the symptomatic treatment of hemorrhage due to precocious menstruation, one can at times apply irradiation to the spleen by the x-rays.

Recently the specific action of thallium has been mentioned. Thallium preparations would be capable of inhibiting the production of ovarian hormones and the process of ovulation. It is also legitimate to employ them in certain forms of hypergenitalism.

The Different Forms of Involution of the Corpus Luteum in Women.—M. Lucien. (*Rev. franç. d'endocrinol.*, 6 : 353, Oct., 1928.)

In the ovary of the human female the regression of the corpus luteum takes place according to two special forms, terminating in the simple fibrous evolutive corpus luteum and the degenerative fibrous corpus luteum or corpus albicans. The involutive fibrous corpus, which may be considered as the normal termination of the lutein involution, results from the banal hyperplasia of the connective elements of the corpus luteum evolving simultaneously with the fatty degeneration of the epithelial cells which atrophy and disappear. This fibrous corpus is but an ephemeral duration and does not take long to amalgamate with and disappear in the ovarian stroma.

The degenerative, fibrous corpus or corpus albicans appears following the brusque involution of the corpus luteum; it is preceded by the necrobiotic degeneration of the epithelial elements and is manifested suddenly by the precipitation of fibrils amid the collagenous protoplasmic ground constituted by the mortified cells. It is the result of a metamorphosing degeneration. The corpus albicans, which has become a foreign body in the stroma of the ovary, remains there permanently. The formation of the corpus albicans may be considered as a pathological phenomenon in relation to the disturbances of ovarian vascularization. Similar processes of involution of the corpus luteum are of a nature to disturb the normal rhythmic functioning of the ovary and to result in quite a series of pathological manifestations in the genital apparatus of women.

Pharmacologic Investigations concerning the Effects of Placenta Extract.—S. Kosakae. (*Japan J. Obst. and Gynec.*, **11** : 27, 1928.)

The author carried out experiments with a placenta extract and a preparation prepared from human placenta through hydrolysis

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splitting by means of acid. Both extracts had a stimulating effect on the surviving uterus of the rabbit and occasioned rise in tonus and increase of the pendulum rhythm in the surviving intestine. Moreover, through the action of this extract, respiration is increased, the blood pressure in the pregnant animal is raised, otherwise lowered. The author believes that he may conclude from his experiments that placenta extract presents a stimulation to the parasympathetic nervous system.

Thymus Gland. — Nitschke. (*Münch. med. Wochenschr.*, **75** : 1782, 1928.)

The author believes that he has obtained an active thymus extract from the thymus, which calls forth the complete picture of tetany, in animals. In addition a second substance may be obtained which markedly lowers the calcium content of the blood.

Concerning the Substitution Theory in Addison's Disease. — Lange. (*Münch. med. Wochenschr.*, **75** : 1740, 1928.)

Following animal experiments with injection of adrenal cortex extract, the author tried clinically the effect on patients with Addison's disease. In the patients he did not use extracts but the material used for the preparation of the extract, administered orally. The first patient had the complete symptom complex of Addison's disease and so great an adynamia that he could only remain out of bed a short while. In 8 weeks of treatment, in which 5 grams of substitution preparation were given daily, an essential change slowly occurred in the patient's condition. There was a gain in weight of 5 kg.; the adynamia disappeared entirely; the patient took walks of several hours duration without interruption or fatigue. The accumulation of pigment in the skin and mucosae definitely decreased. In a second patient under treatment for the past 3 weeks, a gain in weight of 2 kg. and an indisputable lessening of adynamia were noted.

Hyperthyroidism and Diabetes. Considerations concerning Diagnosis and Treatment. — Carrasco Formiguera. (*Med. Ibera*, **22** : 419, Nov. 3, 1928.)

In the author's personal series, which comprises 1,450 diabetics, there are at least 33 in which the existence of hyperthyroidism was suspected; 23 in which this disturbance was clinically very probable and 20 cases of certain diagnosis. Of these 20 cases there are three in which the nature of the glycosuria may not be diabetic; there remain, therefore, 17 cases of coexistence of hyperthyroidism and diabetes.

The author limits himself to some considerations on diagnosis and treatment. In the presence of a case of hyperthyroidism, diabetes must be thought of and an investigation made for glycosuria and induced hyperglycemia, in order to rule out non-diabetic glycosurias. If the curve of hyperglycemia is of diabetic type, it is a case of true diabetes.

The author has the impression that it is of frequent occurrence to fail to diagnose hyperthyroidism in patients qualified as diabetic. He refers to those cases of hyperthyroidism which do not present exophthalmos, or do not present visible goiter, but nevertheless a slight enlargement in size of the thyroid. In these cases in which nothing attracts the attention of the clinician, it is necessary to be guided by the sensation of asthenia and by the loss of weight which can not be explained by the diabetes, since digestive disorders, irritability, exaggerated emotivity, a tremor and tachycardia are frequently attributed to the diabetic condition.

The ideal procedure would be for the physician to systematically determine the basal metabolism in diabetics; but as this is possible only in the great centers of clinical investigation, the physician must search for some of the above mentioned symptoms of hyperthyroidism and in case he finds them, make a determination of the basal metabolism, the sole method of establishing the diagnosis with certainty.

One of the findings which has most frequently suggested hyperthyroidism to the author has been the persistence of loss of weight and strength or the failure to gain even after treatment of the diabetes has brought about a disappearance of the glycosuria with a sufficient diet to obtain a good state of nutrition.

In order that the basal metabolism test may have its full value, it is necessary that this test be carried on when the patient is not glycosuric and has been submitted to a diet that is not loaded with proteins and sufficient to cover the nutritive needs (which can be foreseen independently of the hyperthyroidism). Insulin has made it possible to completely eliminate the unfavorable influence

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of diabetes on hyperthyroidism; so that the prognosis will depend solely on the degree of thyroid disturbance.

Treatment consists in (1) eliminating or reducing to a minimum the factors which in addition to hyperthyroidism may be the cause of the raised metabolism. For which reason it is necessary to avoid the action of cold, to limit as much as possible muscular exercise and reduce the protein diet to the lowest limit compatible with the balanced nitrogen intake; (2) administering sufficient food to cover the energy requirements of the organism, abnormally raised by the hyperthyroidism; (3) increasing as much as possible the metabolic capacity of the organism, for which the necessary quantity of insulin is administered for the necessary amounts of glucose to be tolerated.

In the great majority of cases the adoption of these methods has as effect the rapid and more or less considerable improvement of the general condition, increase in weight, in strength, or at least maintenance of weight, decrease of tachycardia, and nervousness. At times this improvement of the general condition becomes very important.

As the plan of treatment described does not influence the hyperthyroidism at all, the result is that any increase in muscular activity or any decrease in the supernormal amount of food causes loss of weight and of strength and change for the worse in the general condition. In no case did insulin cause any improvement in the thyroid disturbance. For this reason, thyroidectomy, irradiation or anti-thyroid organotherapy will be necessary, according to the case. The author believes that in the majority of cases the better transition for the latter treatments is to be obtained by the administration of small doses of iodin.

Liver Extract and Tropical Anemia. — A. Díaz Albertini and J. Rodríguez Pérez. (*Vida Nueva*, **22** : 191, Sept. 15, 1928.)

The authors report the results they have obtained in many cases of tropical anemia by treatment with liver extract, four cases being reported in detail. The study of these cases again shows the remarkable action of liver in these anemias. Under the influence of liver the number of red blood cells increased considerably and at the same time the proportion of hemoglobin increased. In consequence, the general state of the patients improved notably, the diarrhea disappeared from the very beginning of the treatment and the tongue soon resumed its normal aspect. The authors kept control of the blood sugar of the patients, because experience has shown that by maintaining it at figures around 90 mg. per 100 cc. of blood, the most favorable results are obtained, and because in this way the appetite is stimulated and the protein diet may be amplified by the addition of carbohydrates (but not by fats which are poorly tolerated). In general, five units daily of insulin sufficed.

The authors call attention to the low monocyte count in advanced cases. These increase in number as the improvement becomes more marked and remain in relatively high figures among the normal.

On the other hand, the lymphocytes show a general decrease in number, coinciding with the improvement noted in the processes, and in consequence, they have great importance from the viewpoint of prognosis.

The authors have not yet had sufficient experience with the therapy to speak of the future of these individuals. They can not tell whether the patients will have to continue taking liver extract indefinitely or whether the results obtained will be maintained causing the reactivation or a permanent improvement in the functions of the liver and perhaps an anatomic regeneration equivalent to a cure. At the present time, the authors believe that permanent improvement may be obtained in young individuals. This is not the case in older patients whose completely exhausted liver must be substituted for, and logically the liver treatment will have to be continued indefinitely in these cases.

In concluding, the authors state that a liver preparation with these properties constitutes a considerable advance in modern therapy. Next to insulin, it is the most beneficial force which has been realized in the field of medicine.

With liver extracts the authors have been able to obtain brilliant results in cases where a short time ago there would have been no successful therapeutic agent.

Movement of Water in the Organism. — Mautner. (*Deut. med. Wochenschr.*, **54**: 1824, 1928.)

The movement of water in the organism is dependent upon physico-chemical reactions, muscle contractions, etc. In the gastro-intestinal canal in which not only absorption

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but still more secretion of water takes place, it is the contractions of the intestinal villi which essentially influence the processes of water movement. Yeast extracts, for example, stimulate here. On the other hand, secretion and peristalsis influence the absorption. Nervous stimuli and hormones, for example, the absorption-favoring insulin by way of the hypoglycemic attack and pituitrin, further or restrain absorption. Concerning the complicated processes in the passage of water over into the blood, little is known. The mechanical pressure in the capillaries is decisive for the mechanism of the extravasation of water into the tissues. The essential regulation site lies in the liver, in which the contraction of the liver veins inhibits or enhances. In contraction of the liver veins there may result extravasation of water from the capillaries to the veins, so that following a drink of water a dripping on to the liver surface can be observed. Here also not purely mechanical but also hormonal influences are at work. In the kidneys too not only filtration or expressing but also vital processes and nervous influences are active. In perspiration an inactive phase likewise must be assumed through which the water can enter through skin or lungs. The water deposits are also involved in the regulation of the water stability, the activity of which is restrained through a regulating center. A diuresis inhibition proceeds from the cerebrum; the diuresis center lies in the vicinity of the tuber cinereum, of which one part is connected with the pituitary. Pituitrin, which streams directly into the third ventricle, acts as a stimulus for the part of the diuresis center situated here. The adequate stimulus for this center is probably the oncotic pressure of the circulating albumin and the changes of the blood albumin picture. In addition, nervous influences, salt content and reaction of the blood and above all glands with internal secretion play a rôle.

Clinical Value of the Ovarian Preparation Prepared According to the Method of Stern-Batelli. — A. Kogan and L. Libin. (*Arch. Gynäkol.*, **135** : 262, 1928.)

The frequent lack of result in the use of ovarian preparations encountered commercially may be explained by the fact that the ovaries like other endocrine glands, possess no store of specific hormones, but secrete them in the quantity in which they arise in the blood. An active preparation could therefore only be prepared when the gland concerned continues to live following its removal from the organism and can secrete its secretion products into the environs. The method of Stern-Batelli rests on this principle: the ovaries were cut into fine pieces, placed in Ringer's solution previously warmed to 38° and saturated with oxygen; 10 cc. of Ringer's solution to every 1 gm. of tissue. The tissue remains 20 to 30 minutes suspended under a supply of oxygen at body temperature; the fluid is frequently changed. Finally, the whole fluid is filtered and used without further treatment. For the most part, 50 to 100 cc. were administered once or twice daily per rectum. The preparation was given in 62 cases. In 12 women of 22 to 43 years, in whom the uterus and ovaries had been removed, and severe deficiency symptoms existed, increase of deficiency symptoms appeared during the first weeks of treatment, followed, however, by essential improvement. These women had previously been treated with organ preparations altogether without result. The same thing occurred with 8 patients in the climacteric with symptoms of ovarian insufficiency, in whom improvement was obtained through the preparation. Moreover, 22 women with amenorrhea (in part with underdevelopment of the genitals) were treated with this preparation. These women had also been treated previously without result with organotherapy. With the Stern-Batelli preparation regular menstruation was obtained in one part of these amenorrheic cases. Finally 16 patients from the Neurological Clinic (12 basedowoid and 2 with pronounced exophthalmic goiter) were successfully treated with this preparation. In order to effect complete stimulation of the ovaries a 4 to 6 weeks treatment is necessary.

Modern Treatment of Diabetes in Children.—R. Wagner. (*Wien. med. Wochenschr.*, **78** : 1139, 1928.)

If the diagnosis of diabetes has been made in a child, then insulin should be given at the outset even if sugar can be removed without insulin. For in the first place it is easier with this therapy to get rid of an infection to which the children are frequently exposed and secondly, with simultaneous treatment with insulin, more carbohydrate may be given to the child, which is of great

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importance in childhood: If a child is received in coma, 50 to 60 units are given intravenously as initial dose and the injections are repeated in small doses every 2 to 3 hours within the first 12 hours. When vomiting has ceased and respiration has improved, the doses of insulin must be lessened in order not to induce hyperinsulinism. Small children are very sensitive to insulin and easily become hypoglycemic. In this case, when an oral administration of sugar is not possible, 10 per cent glucose solution is given subcutaneously.

Acrocyanosis of Young Women. The Physiopathologic and Pathogenic Importance of Venous Hypertension and Ovarian Insufficiency. — M. Villaret and F. Saint Girons. (*Arch. Méd. Enf.*, **32** : 79, Feb., 1929.)

The authors have observed the existence of a syndrome characterized by three factors in a rather large number of patients ranging from 15 to 20 years: acrocyanosis, ovarian insufficiency and increase of venous tension. The young women have had irregular menstrual periods from the beginning of menstruation; obesity is at times important and is generally distinct. All present a very marked cyanosis of the hands, less marked of the feet, with edema and chilling; the disturbances are very marked during the winter where they terminate in painful frostbites; these frequently ulcerate and resist the classic treatment as long as the weather remains cold. Otherwise, the patients give no clinical sign of disorder or anomaly of the circulatory, respiratory, urinary or nervous system. However, in contrast to a maximum normal arterial pressure, their venous pressure is constantly increased.

It seemed to the authors that this syndrome was intimately related to the existence of ovarian disorders as shown by the irregularity of menstruation and the frequent obesity. It is a question of endocrine cyanosis, for ovarian organotherapy has given definite results, especially in one case (improvement of the subjective disturbances with improvement in the menstrual periods, indisputable decrease of cyanosis and slight fall of venous pressure).

The authors do not wish to give the impression that all cases of acrocyanosis are of ovarian origin but merely wish to show that some cases of this disturbance have this etiology. It appears also that the ovarian disorders which are the cause of the cyanosis and venous hypertension are solely disturbances of hypofunction. In fact one woman whom the authors had occasion to observe was suffering from obesity of thyro-ovarian origin with vertigo, headaches, sweating, increase of menstrual flow, and presented severe metrorrhagia whenever ovarian therapy was attempted. In this case of hyperovarianism the venous tension was not only not increased, but was distinctly below the maximum arterial tension.

The interest of the syndrome resides especially in its pathogenesis. Venous hypertension need not be dependent upon a cardiovascular affection alone but may also result from an endocrine alteration. It is also worthy of notice that the venous hypertension and acrocyanosis may decrease in parallel manner under the action of ovarian therapy.

Spleen and Rickets. — R. Soula and Cauquil. (*Paris méd.*, **18** : XIII, 1928.)

Rickets can only be an endocrine insufficiency of elaboration of sterins. This elaboration which under normal conditions probably takes place through the spleen and reticuloendothelial system, is insufficient in rickets. It can be corrected through irradiation and organotherapy.

Pituitary Dwarfism. — Dr. and Mme. Schiff. (*Paris méd.*, **19** : xxx, Jan. 5, 1929.)

The authors present a patient of 14½ years whose physical growth has been completely arrested since the age of nine years. At that time a syndrome of cranial hypertension expressed itself in intense headaches and vomiting. Two years later, the child became suddenly and totally blind. The headaches have persisted since that time. At the present time there exists a complete atrophy of the optic nerves, a slight hydrocephalus, a considerable enlargement of the sella turcica upon radiography. Outside of the dwarfism a fall of basal metabolism of 26 per cent and a testicular sclerosis were noted. The Bordet-Wassermann test of the blood was negative in the subject and his mother. Specific treatment prolonged for 4 years, remained ineffective.

The authors discuss the indication for a surgical intervention (transphenoidal ablation, transfrontal puncture), despite the irremediable loss of the vision, and the

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utility of the radiotherapy, which would have to be very prudent because of the great radiosensibility of the nervous cells of the child.

Painful Vasomotor Disorders in a Case of Dysendocrinism. — M. Scharrenberger. (*Presse méd.*, **37** : 146, Jan. 30, 1929.)

The patient, a young man of 20 years, presented painful pricking of the hands and feet; at times, paroxysmal pain accompanied by pallor and coldness of the fingers and toes; at times cramps. Beginning at the age of 10, the present condition has existed since the age of 14 years. The disturbances came on without apparent cause. The subject was never able to do any appreciable work.

On examination there was noted a feminine habitus, a dysthyroidism and signs of sympathetic disequilibrium. The patient's hands were smooth, pale in color, warm to the touch, of weak muscular strength in proportion to the slenderness of his extremities, without pyramidal deficiency. Normal objective sensibility; no pain on pressure. In short, an association of endocrine sympathetic signs in a young man presenting painful vasomotor symptoms.

Concerning Hyperglycemia in Acute Disease of the Pancreas. — F. Bernhard. (*Deut. Zeitschr. Chir.*, **212** : 217, 1928.)

Hyperglycemia is an important symptom of acute disease of the pancreas. The cause of hyperglycemia is to be attributed to lack of insulin. For this reason, energetic insulin therapy is recommended in acute necrosis of the pancreas.

Investigations concerning the Influence of the Thymus on Muscular Activity. — O. Held. (*Zeitschr. Biol.*, **88** : 76, 1928.)

The author performed experiments with thymus extracts which were injected part subcutaneously, part intravenously and tested the influence of thymus preparations on the phenomenon designated as "apparent fatigue." This apparent fatigue is removed, as this experiment shows, by subcutaneous and intramuscular injection of thymus preparations. It is not the effect of an albumin substance. The action of thymus preparations is shown on the working muscle itself, whose ability for work is heightened. Control experiments with Ringer's solution were negative. Intravenous injection of adrenalin solution did not have the same effect as thymus preparations.

Studies of Calcium Metabolism in Certain Diseases of the Skin. — N. Burges. (*Brit. J. Dermat. and Syph.*, **40** : 279, 1928.)

Certain dermatoses are dependent on increased irritability of the nerve cells, caused by lack of calcium in the tissues. The results of treatment show that administration of calcium and thyroid preparations in dermatoses of nervous origin is of special value. Cases of urticaria, prurigo, eczema and those cases of cyanosis of the extremities and chilblains with low calcium content of the serum were considerably improved with calcium and thyroid therapy.

Hormonal Influencing of Sex in Animal Experiment. — Beyer. (*Med. Welt*, **2** : 1528, 1928.)

Resuming the experiments of E. Vogt, Beyer remarks that to the two possibilities of influencing sex — through undernutrition and overnutrition — the hormonal influence may be added as a new possibility. Through this the general law is supplemented, according to which in times of need, under abnormal living conditions more female young are born than male. In this way the preservation of the species is most certainly guaranteed. From this viewpoint the hyperfeminization of the new generation seems to be a sequel to the injuries undergone during the war.

Influence of the Glands with Internal Secretion in the Metabolism of the Bones. — Biedl. (*Med. Welt*, **2** : 1544, 1928.)

In embryonal life and shortly after, the interrenal system (adrenal cortex) and the sex glands are especially influential, on the contrary, the thyroid minimal. In the phase of puberty, the time especially of growth in length, thyroid activity appears in the foreground, and raises the metabolism. Here we also have hyperthyroid disturbances, the goiter of puberty. The proper growth glands are the thyroid and the pituitary anterior lobe. However, without the growth symphyses remaining open, growth is not possible and the symphyses remain open only so long as the development of the sex glands is not yet complete. Administration of thyroid

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substance can occasion changes in growth and proportions even in adults. The hyperthyrosis causes an excessive growth in length in the growing individual. Pituitary dwarfism can be improved by administration of pituitary substance. The pituitary anterior lobe is a growth gland. Premature development of the sex glands can also be influenced by feeding of pituitary.

Neuroses Conditioned by the Endocrine Glands. — F. Boenheim. (*Arch. Verdauungskrankh.*, **42** : 383, 1928.)

The author contributes histories of patients and disease pictures in order to draw the attention of physicians to the etiological significance of endocrine disturbances for neuroses, psychoses and hysterias. The recognition succeeds only through exact somatic investigation with respect to the endocrine function. The thyroid probably produces a whole series of different hormones so that in dysfunction of the thyroid the most diversified disease pictures can arise. Boenheim sees a corroboration of his conception of the endocrine genesis of many neuroses in the therapeutic activity of specific organotherapy, for example, whole pituitary suppositories.

A Case of "Ovarian Diabetes," Resistant to Insulin, Very Much Improved by Folliculin. — Carnot, Terris and Caroli. (*Bull. et mém. soc. hôp. Paris*, **44** : 738, 1928.)

A 36 year old patient, in whom diabetic symptoms and amenorrhea arose simultaneously. Daily excretion of sugar up to 100 gm., at times acetone, marked emaciation, distinct variations with the menstrual cycle. Neither dietetic nor insulin therapy had any effect. Following injections of folliculin, decrease of urine and blood sugar. Gain in weight.

Rise in Blood Pressure and Extirpation of the Spleen. — Hercher. (*Zentr. Chir.*, **55** : 2350, 1928.)

The author refers to the repeatedly observed threatening fall of blood pressure, which appeared following the use of spleen extract. The question whether it is a matter here of a hormone action or an anaphylactic manifestation is not yet clear. Can the rise in blood pressure following extirpation of the spleen be considered as an effect of removal of the organ, perhaps conditioned by a loss of an internal secretory principle of the spleen?

Internal Medicine and Chemistry. — H. Horsters. (*Med. Klin.*, **24** : 1441, 1928.)

A new branch of chemical therapy has arisen with the discovery of adrenalin: hormone therapy which can also be designated as constitutional therapy. Here medical chemistry in clinic and laboratory has celebrated triumphs with the discovery of insulin. In synthetic thyroxin a further important step in this field has been made. Liver therapy in pernicious anemia promises new discoveries in the ranks of substitution therapy. The important task is here reserved for the chemist to isolate the sum of the active principles and present it pure. The closest joint work with the clinic is indispensable for the experiment. In respect to the purification of organ extracts, however, nature orders a halt, according to all appearances, in that it has been shown that in a part of these substances a too extensive purification in the sense of the isolation of a chemically defined substance often leads to decrease of activity. In this connection the work on insulin must be remembered.

Diuretics. — A. Herz. (*Wien. klin. Wochenschr.*, **41** : 1378, 1928.)

Thyroid preparations act extrarenally in dropsy with lowered thyroid activity and in nephroses. Their use is contraindicated in cardiac edema, in nephrosclerosis, hematuria and hyperthyroidism. Control of the pulse and of the properties of the urine is absolutely necessary in thyroid medication. Thyroid tablets should be given in a dosage of 0.3 gm. at the beginning increasing to 2 gm. after about 2 weeks.

Practical Therapeutics

(*Continued from page 145*)

anism of action as the continuous absorption of minute amounts of nitrite ions, thus causing gradual relaxation and rest. He summarizes as follows:

"1. Variations in the chlorid content of the blood do not affect the arterial tension to any major degree.

"2. Administration of bismuth subnitrate causes a slight reduction in the chlorid content of the blood, as do other nitrates, through the production of a chlorid diuresis.

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"3. Administration of bismuth subnitrate assists materially in obtaining a reduction in arterial tension in hypertension, both in non-pregnant and pregnant cases.

"4. The therapeutic results are much better when arteriosclerosis is not marked.

"5. A method of evaluating therapeutic results in hypertension in terms of percentage return to normal is presented.

"6. The pharmacodynamic mechanism of bismuth subnitrate in hypertension is a dual one:

"*a.* Gradual vasodilation by continuous absorption of small quantities of nitrite (NO_2^-) ions.

"*b.* Reduction of the blood chlorid content by diuresis initiated by the nitrate (NO_2^-) ions.

"7. The fundamental value of bismuth subnitrate in hypertension lies in its property of breaking the vicious circle of vascular fatigue, hyperirritability, with more spasticity and fatigue and thereby permitting of physiologic *rest.*"

Hypertension is of unknown etiology as far as the ultimate causes go. The treatment, therefore, is partly symptomatic and expectant. Perhaps no condition claiming the attention of a physician requires so much individual study. The careful physician, however, can accomplish much in most of his cases.

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A Case of Intersexuality of Hermaphroditic Type. — G. Marañón. (*Med. Ibera*, 22 : 381, Oct. 27, 1928.)

The states of intersexuality in the clinic may be divided into the following groups: hermaphroditism, masculine or feminine pseudo-hermaphroditism, virilism and feminism, cryptorchidism and hypospadias, gynecomastia, homosexuality and other functional intersexualities, intersexualities of puberty and the climacteric, partial intersexuality in normal subjects. Of all these types of intersexuality, the most unusual is hermaphroditism. Nevertheless, it is probable that the true hermaphroditism, that is, the simultaneous presence of two sex glands in the same individual with the corresponding coexistence of the characters of both sexes, is much more frequent than supposed. In fact, in order to be certain of the existence of the mixed sex glands or ovary-testis, it is necessary not to limit oneself, as is generally done, to the examination of a single genital gland extracted during a surgical intervention, but the two glands must be studied carefully, since in the majority of cases the ovary-testis is limited to a single side and perhaps to one of the poles of the sex glands. For this reason, various cases diagnosed as pseudo-hermaphroditism, that is, of inverted appearance with normal sex glands, must be in reality true hermaphroditism incompletely studied. To this group belonged without doubt an intersexual who was exhibited at fairs in Spain and who was recently studied in the author's clinic. He is sixty years old and reports that he has menstruated up to about fifty years. His appearance is mixed. The distribution of fat, the comparative proportions of his pelvis, and scapular girdle, the pubic hair and above all the breasts are those of a woman. The hair and voice are masculine. He states that his instincts are also virile and that he has had frequent sexual relations with women. The genital organs show a penis the size of that of a boy of about 15 years, without urethra. This opens one centimeter below, and 2 cm. lower a small vaginal conduit opens. The labia majora have the appearance of empty scrotal sacks.

This case would usually be diagnosed as one of feminine pseudo-hermaphroditism; Pozzi labeled it such 26 years ago. The equal presence of both sexes, however, suggests a case of true hermaphroditism. In this case, however, as in others, an exact diagnosis could only be made after histological examination of the sex glands.

General Therapy of Skin Diseases. — Otto Kren. (*Wien. klin. Wochenschr.*, **41** : 1404, 1928.)

Organotherapy attempts to improve the function of diseased organs, or to replace

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their chemical function. As is well known, the endocrine glands also secrete substances peculiar to them, of which each one has a very special task to fill for itself in the body. These substances are the hormones. To carry out a correct hormone therapy, signifies being acquainted with the action and symptoms of abolition of function of the endocrine glands with their effects on the skin and the organism in general and treating them accordingly. In this respect it is to be mentioned that frequently not only one gland is disturbed in its function but the whole harmonious interrelationship of all glands, that, therefore, obviously several glands are functioning abnormally and for this reason call forth a disturbance.

Pulvermacher recently reported investigations, therapeutic results and experiments and arrived at results full of contradiction. One is, however, certain: Each of the endocrine glands can produce substances in disturbed function which sensitize the integument and so give occasion for the origin of a dermatosis. Whether the secretion itself forms a hormone, as is claimed by some authors, which is also involved in the course of the dermatosis, must be determined by further investigation. The type of treatment consists for the most part in the administration of the missing hormones or in roentgen stimulation of the organs concerned. In the administration of the hormone the subcutaneous or intravenous form of administration is in each case superior to the oral.

Animal Experimental Investigations concerning the Pituitary Anterior Lobe Hormone with Special Reference to the Reproductive Phases. — Schultze-Rhonhof. *Deut. med. Wochenschr.*, **54** : 1702, 1928.)

Typical changes are found in the vaginal mucosa even in castrated animals 72 hours following injection of ovarian preparations. Pituitary anterior lobe implant in still immature mice results in sexual precocity in 80 to 100 hours and simultaneously to change of the vaginal mucosa. In castrated animals, pituitary anterior lobe has no influence. In an infantile mouse even the implantation of the pituitary of an 80 year old individual had a marked influence. Infantile hypophyses implanted into infantile animals likewise result in signs of pronounced ovarian function, even when the implant came from animal fetuses; human fetal organs acted only to 50 per cent. Through simultaneous implantation of anter... pituitary and thymus, the origin of est... was for the most part prevented.

Relations between the Digestive Tra... and Blood Diseases. — Schottmüller. (*Me... Welt*, **2** : 1538, 1928.)

Liver powder gives the best results. I... "liver remissions" increase in reticulocyte... occurs after 1 week; after 8-14 days increase... in erythrocytes and hemoglobin occur. T... manner of action of liver is still unknown— hormonal or detoxicating? Analogous to liv... therapy in pernicious anemia, spleen trea... ment is to be tried in hyperglobulia.

Arthur Hartmann

(*Continued from page 147*)

and relating to physicians. He attended meetings of many medical societies at which he sometimes contributed and sometimes presided; he abstracted material for these meetings as well as for several publications in which he took an interest. The journey to England and France was a kind of self-imposed apprenticeship through which he was able to bring to his own country the best knowledge and experiences of the workers in other countries. He served on Medical Boards in both active and advisory capacities. The desire to reform and improve medical study prompted Hartmann to make a survey of courses of instruction for physicians especially in England and France and also in other countries of Europe. He presented his findings in several essays and drew up a new system for Germany. As a member of the *Schuldeputation* in Berlin and as an official in charge of City Hygiene, Hartmann instituted a course of special training for school doctors, for it was his belief that physicians must be especially trained to handle children. He assisted in establishing a school for the instruction of deaf and dumb individuals based on the principles derived from his researches in this special field.

As evidence of a practical bent, there are several instruments invented by Hartmann, for use in the treatment of diseases of the ear, nose and throat. They are still in use under his name.

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The Theory of Insulin Action. — Schur. (*Klin. Wochenschr.*, 7 : 1983, 1928.)

Schur is of the opinion that insulin attacks the assimilation process in such a way that it effects the deposition of carbohydrate in the fat tissue and its transformation into fat tissue. Proceeding from this standpoint, the author undertook determinations of the total carbohydrate in the fat tissue with a new method, according to Dische and Popper, and constantly found quite considerable amounts of carbohydrate as well as a quantitative influencing of it through administration of carbohydrate. Insulin probably also has a direct effect on the deposition of lipoids. It appears, therefore, quite generally to have a furthering influence on the deposition of food substance ingested.

Porges, Vienna, proceeding from the viewpoint that even in normal individuals a diet rich in carbohydrate raises the carbohydrate tolerance, gave diabetics a diet rich in carbohydrate (with the use of large doses of insulin), thereby a diet rich in albumin but poor in fat with a considerable increase in tolerance as a result.

Discussion: Adlersberg is of the opinion, according to his experiments, that the retrogression of the urinary sugar in this form of diet is dependent upon an increased density of the kidneys. Minkowski, Wiesbaden, doubts this and considers the rise in tolerance obtained to be dependent upon the large amount of insulin used. Porges stresses that the rise in tolerance is also obtained without insulin and even with the use of insulin appears only when abundant carbohydrate and little fat are given, not, however, when little carbohydrate and a large amount of fat are given.

Nature and Treatment of Hyperemesis Gravidarum. — Runge. (*Zentr. Gynäkol.*, 52 : 2547, 1928.)

Insulin is no longer to be dispensed with in the treatment of hyperemesis. It is, of course, understood that care must be taken that carbohydrate be administered before the injections, either in the form of sugar water or, when that is not tolerated, in the form of rectal injections. To overcome the severe conditions of emaciation in this disease, insulin forced feeding offers quite an essential support in doses of about 5 units. The appetite increases, there is gain in weight. There is no question but that insulin is an extraordinary adjuvant to therapy in this condition. Runge is altogether of the opinion of Heynemann with respect to the specific action of insulin. It is as little a question of a specific effect in the insulin effect here as in any other remedy used up to the present in hyperemesis.

Action of Thyroxin on the Heart. — M. Nothmann and G. W. Parade. (*Klin. Wochenschr.*, 8 : 699, 1929.)

The sharply defined relationship between hyperthyroidism and cardiac symptoms, as well as the great rôle claimed by thyroid gland therapy due to artificial incorporation of thyroid gland incretion by the method of Kendall and Harrington, gave the authors the impetus to investigate the action on the heart of doses of thyroxin administered intravenously and perorally. They used for the experiments synthetic thyroxin derived according to Schering and employed the method of Schoeller. In the metabolism experiments conducted by Lublin, it was seen that this preparation acted to increase the basal metabolism.

The effect of thyroxin was observed on the healthy heart and on a series of cardiac patients. Report will be made later concerning their tests on thyroid gland patients.

In twenty patients, neither after intravenous (two doses, 5 mg. per dose) nor in *per os* administration (three times daily, 1 mg., 2-4 weeks duration) did they see any signs of hyperthyroidism whatever. The general condition was in no way disturbed.

The pulse frequency in persons with healthy heart showed, similar to the investigations of Baur and Loewe, no increase, if we accept as a psychic factor the rare occurrence of 10 beats increase per minute immediately after injection. Likewise irregularities of pulse were never induced. In three cases of absolute arrhythmia, a striking increase in frequency was observed after injection of small doses, which was less conspicuous after large doses. With intravenous injection of large doses the author was under the impression, often, that the pulse was noticeably slower.

The most important of the authors' investigations are concerned with the effect of thyroxin on the course of the electrocardiographic curve. In their normal cases neither was there any effect to stimulate the heart itself nor any other part of the body. The configuration of the auricle or ventricle complex was never altered. In cases of auricular

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flutter or auricular fibrillation with absolute arrhythmia of the ventricle the authors observed no increase in the fibrillation symptoms of the cord. After small intravenous doses of thyroxin, the often improved, increased discharge of the ventricle, running parallel with a striking increase in pulse frequency, was seen which can be spoken of as a cursory improvement of transfusion. In one case of entire dissociation based on luetic cardiac affection, neither was the sinus frequency increased nor were the secondary centers of the ventricle affected.

In conclusion, the authors state that thyroxin, of the forms of medication chosen by them, does not act on the pulse frequency or the course of the electrocardiographic curves.

Castration in Pregnancy. — Waldstein. (*Wien. klin. Wochenschr.*, **42** : 380, 1929.)

Both ovaries were removed from a woman with bilateral dermoid cysts in the second month of pregnancy, a normal termination of birth resulted in a child weighing 3500 gm. taken by forceps. The case was subjected to quite elaborate hormone study. The ovarian hormone content of the blood serum was quite like that of normal women. In desiccated extract of the placenta about 300 mouse units of ovarian hormone were determined, a rather insignificant amount, but as the investigations on the subject show, it can be indicated as normal, since even in normal placentas a similar amount can be found. From the above experiments the following conclusions were obtained:

1. Ovarian hormone does not originate in the ovary, but rather in the placenta.
2. The placenta does not store the hormone.
3. The hormone produced from the placenta was given into the blood *in statu nascendi*, for as much ovarian hormone could be found in the blood of the placenta as occurs in the whole placenta. By means of these investigations the theory of Halban appeared to be confirmed, whereby the placenta produces "active substances." This is none other than hormone.

The hormone of the anterior lobe of the pituitary was likewise evident after castration, as well as in other pregnant women, so that one can assume that production of the hormone of the anterior lobe of the pituitary was not affected by castration. From the urine of castrated women much less ovarian hormone was isolated than from that of normal pregnant women. The author believes in treating the castration symptoms after the termination of lactation with the hormone derived from the woman herself.

Four weeks after the castration operation the woman suffered a psychosis, for which she was promptly hurried off to a psychiatric clinic.

Sex Hormone in the Urine of Pregnant Women. — Leiv Kreyberg. (*Norsk Magasin for Laegevidenskapen*, **90** : 379, 1929.)

Ovarian hormone as well as pituitary hormone can appear in the urine. Ovarian hormone is found in the urine in a whole series of body conditions: in pregnancy, at the beginning of the climacterium as well as in certain forms of amenorrhea. In contrast to this, the pituitary hormone appears spasmodically, as it were, in the urine of initial pregnancy and can therefore serve as an efficient indication of early pregnancy. The author adds observations from which the changes in infantile sex organs of the mouse due to pituitary hormone from the urine of pregnant women are indisputable.

Concerning Specific-Dynamic Activity and Pituitary (Rat Experiments). — R. Nothhaas. (*Pflügers Arch. ges. Physiol.*, **221** : 763, 1929.)

By feeding substance from the cortex of the anterior lobe of the pituitary, a specific-dynamic activity occurred in rats in 14 days to 3 weeks (normal about 20 per cent) to a maximum of about 26 per cent increase. Therewith the basal metabolism fell.

Therefore the rat is a suitable test object with regard to the component of the anterior lobe of the pituitary, which initiates metabolism.

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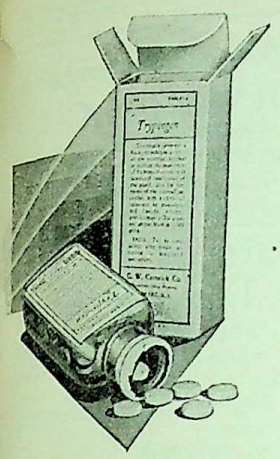
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There was no question about the diagnosis---the patient—female; 22 years; unmarried; office employment; intense dysmenorrhea preceding each menstrual period. Palliative and single gland endocrine therapy ineffective after six months of treatment.

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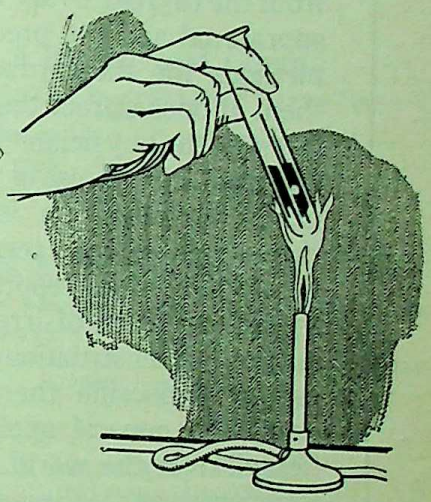
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LABORATORY CONTROL

is desirable in all cases and imperative in grave cases of

DIABETES

BUT---nothing is a substitute for careful clinical observation. It is more important to adjust the diet to the caloric requirement of the patient, administer proper pancreas therapy and maintain a state of well being than to strive by heroic means to quickly remove sugar from the urine and to reduce blood sugar.



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DYSMENORRHEA

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Abstracts (Continued)

Constitutional Weaknesses of the Cardiovascular System in Young Children. II. Constitutional Weaknesses of the Cardiovascular System and Internal Secretion of Young Children. IV. [illegible]

Hydrops Articulorum [illegible]

Concerning the Various Actions of Histamin and Adrenalin on the Blood Vessels in the Rabbit's Ear [illegible]

Circulatory Problems [illegible]

Therapeutic Application of the Hormone of the Circulation [illegible]

Embolism and Thrombosis [illegible]

Concerning the Relationship of Pituitary Gland and Hypothalamus to the Retention of Water [illegible]

Folliculin, Insulin and Diabetes [illegible]

The Basal Metabolism [illegible]

Relations between the Digestive Tract and Blood Diseases [illegible]

The Internal Secretion of the Salivary Glands [illegible]

Endocrinology and Opotherapy [illegible]

Skin and Venereal Diseases [illegible]

Concerning the Rôle of Adrenalin, of Insulin and Glycogen Sugar on the Mechanism of Attacks of Angina Pectoris [illegible]

Concerning the Action of Post-Pituitary Extract on the Musculature of the Uterus [illegible]

Concerning the Influence of Administration of Thyroid Gland on Albumin and Fat Metabolism [illegible]

The True Acidity in Isolated Portions of the Male Genital Apparatus of the Rat and Its Hormone Limitation [illegible]

Transplantation of Preserved Ovary. IV. Transplantation of Desiccated Ovary [illegible]

Investigations on the Origin of Creatin or Creatinin in the Animal Organism [illegible]

Experimental Investigations on Corpus Luteum [illegible]

Hormone of the Anterior Lobe of Pituitary as Related to the Male Genital Tract [illegible]

The Zondek-Aschheim Pregnancy Reaction [illegible]

Organ Extracts in Their Action on Immuno-Biological Processes [illegible]

Insulin and Nutrition Depots [illegible]

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Insulin, Epinephrin and Sugar Metabolism

INSULIN and epinephrin are important factors in carbohydrate metabolism. Their action is opposed and is exerted in the peripheral tissues. Epinephrin increases deposition of liver glycogen, insulin decreases it.

In considering the sugar metabolism of the body, the oxidations which give rise to the energy supply and the manner in which the nutritive material is stored and released for oxidation, the logical starting point is glycogen. Glycogen is a polysaccharid—a storage sugar—and is found in almost all the tissues of the body, but particularly in the liver and muscles. Glycogen is one of the products synthesized in the body, principally from the carbohydrates but also from the proteins and the products of protein cleavage—the amino acids (1). Whether fat may be converted into glycogen is still debatable.

Under ordinary physiological conditions carbohydrate metabolism is characterized by continuous activity in both muscles and liver. As soon as the dextrose of the blood reaches a low level due to oxidation by the cells the deficit is made good by the glycogen of the liver, which, under the influence of the enzymes of the hepatic cells, undergoes transformation into blood sugar (dextrose). The glycogen of the muscles is converted into liver glycogen by a process which has received considerable attention recently and which is now fairly well understood.

Since it was clearly evident that injection of epinephrin gave rise to hyperglycemia and

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glycosuria, and since the greatest sugar values were obtained in animals rich in liver glycogen, it was assumed by early workers in the field that epinephrin reduces the glycogen store of the liver. Evidence began to accumulate, however, that epinephrin may actually cause a formation of glycogen which is deposited in the liver. Pollak (2) found that in starved animals as much glycogen may be formed by injecting epinephrin as by carbohydrate feeding. Kuriyama (3) also reported increase of liver glycogen following epinephrin injection.

J. Markowitz (4) found that "The injection of epinephrin into starved rabbits always evokes extensive hyperglycemia, even when the injections are kept up for days.

"When the liver is glycogen-free, injection of epinephrin does not lead to hyperglycemia. When the liver contains traces of glycogen, hyperglycemia of delayed onset ensues, the extent being proportional to the amount of glycogen.

"Mere starvation does not make rabbits glycogen-free. Starvation in the cold, followed by strychnine convulsions will make the liver, heart and muscles glycogen-free for several hours.

"Repeated injection of epinephrin into starved, strychnine-treated rabbits permits glycogen to accumulate in the liver, heart and muscles.

"When insulin is given to starved strychnine-treated rabbits along with epinephrin, considerable quantities of glycogen, up to 2.77 per cent accumulate in the liver.

"The above experiments together with those quoted from the literature, demonstrate that glycogen is obligatory, and not an optional step in the formation of blood sugar from the non-carbohydrate stores of the organism."

C. F. and G. T. Cori (5) investigated the whole problem of glycogen formation and the effect of both epinephrin and insulin on glycogen and blood sugar. The earlier views of the action of epinephrin assumed a direct action on the glycogen of the liver. Actual little investigation appears to have been made on this point. Since the source of blood sugar was known to be the glycogen of the liver it was assumed rather than observed that the increase of blood sugar and glycosuria following epinephrin injection was due to an action in converting liver glycogen into dextrose.

In Coris' work the assumption was made of an extra-hepatic point of action. Insulin and epinephrin exert opposed actions on blood sugar. Insulin acts by causing mobilization of liver glycogen and there are no differences in rate of disappearance of liver glycogen in normal and adrenalectomized animals following insulin injection. Actually the site of epinephrin action was found to be on the glycogen of the muscles rather than that of the liver. The earlier observations of an increase instead of a decrease of liver glycogen were confirmed. Epinephrin converts muscle glycogen first into lactic acid which is then converted into liver glycogen which therefore increases in amount.

In order to ascertain whether liver glycogen can be formed from lactic acid, δ-lactic acid, its sodium salt and γ-sodium lactate was fed to fasting rabbits with a resulting deposit of glycogen in the liver. This was consonant also with previous work which showed a marked increase of lactic acid in the blood following epinephrin injections. The possibility that epinephrin causes an increase of liver glycogen by conversion of protein to glycogen is dismissed as having less evidence to support it. In the discussion of one of their papers the Coris say:

"According to the generally accepted explanation epinephrine causes hyperglycemia, and after large doses, glycosuria, merely because it mobilizes liver glycogen. As pointed out in the introduction, hyperglycemia and glycosuria can not be explained on this basis because there is not enough liver glycogen present to provide the tissues for hours with sugar at a rate which is greater than their normal ability to utilize sugar. This is illus-

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trated by the following calculation. In the experiments in Table IV the average blood sugar was 174 mg. per cent 3 hours after the epinephrine injection. In order to produce a hyperglycemia of this magnitude in normal rats, glucose must be infused intravenously at a rate of 250 mg. per 100 mg. of body weight per hour (Cori and Cori, *J. Biol. Chem.*, 1927, lxxii, 597). Hence, a mobilization of 750 mg. of liver glycogen or an initial glycogen content of the liver of 20 per cent is required, if the hyperglycemia of 174 per cent is to be explained merely on the basis of glycogen mobilization in the liver. Actually there were only 218 mg. or 5.6 per cent liver glycogen present to start with (Table II), and the liver glycogen showed an increase after the epinephrine injection. This indicates that other factors play a rôle in the production of hyperglycemia besides mobilization of liver glycogen. In fact the experiments with epinephrine in Table IV, when taken at their face value, give no evidence that liver glycogen is being mobilized; only by means of a finer analysis could it be shown that mobilization of liver glycogen occurs.

"Decreased utilization of blood sugar is one of the principal causes for the epinephrine hyperglycemia under postabsorptive conditions. The blood sugar rises after epinephrine injections, because the utilization of blood sugar in the peripheral tissues falls behind the supply of blood sugar by the liver, even if the supply is not much higher than normal. For this reason, amounts of sugar given off by the liver will cause hyperglycemia, amounts, which when injected into normal animals, have no effect whatever on the blood sugar level. Hitherto it has been assumed that a decreased utilization of blood sugar must be associated with a decreased carbohydrate oxidation. The present experiments reveal that after epinephrine injections carbohydrate oxidation is carried on at the expense of muscle glycogen and that the carbohydrate oxidation may be increased in spite of a diminished blood sugar utilization."

"The conversion of lactic acid derived from muscle glycogen into liver glycogen explains why epinephrine hyperglycemia can persist for several hours without causing depletion of the glycogen stores of the liver. A decrease in liver glycogen is to be expected only if glycosuria develops. In rabbits during epinephrine glycosuria more sugar appears in the urine than can be accounted for by the disappearance of liver glycogen, indicating that resynthesis of liver glycogen from lactic acid occurs also in this species (unpublished experiments). It can now be understood why different observers obtained conflicting results when they determined the glycogen content of the liver after epinephrine injections. With small doses of epinephrine, or even with large doses when the glycogen content of the liver is low, resynthesis of liver glycogen from lactic acid exceeds mobilization, and consequently the liver glycogen is found higher after the injection. With large doses and a high liver glycogen the latter diminishes because the loss of sugar in the urine can not entirely be compensated by resynthesis of liver glycogen.

"It is surprising that an extrahepatic action of epinephrine on carbohydrate metabolism has not been emphasized before. The experiments on 24 hour fasting and on rats in the postabsorptive state indicate that the extrahepatic action of epinephrine consists in a mobilization of muscle glycogen. Whether this mobilization is responsible for the decreased utilization of blood sugar, or whether both processes are influenced independently by epinephrine, can not be decided at present.

"Since the end-product of glycogen breakdown in the muscle is lactic acid, epinephrine can not raise the blood sugar level after removal of the liver. However, the influence of epinephrine on blood sugar utilization is demonstrable on hepatectomized animals, as will be shown in subsequent papers.

"Insulin produces hypoglycemia because the supply of sugar falls behind blood sugar

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utilization, in spite of a rapid mobilization of liver glycogen. Epinephrine and insulin antagonize each other on account of their opposite effect on blood sugar utilization in the peripheral tissues."

The experimental work showed that in control rats 216 mg. of glycogen disappeared in 3 hours time: 23 per cent was derived from the liver, 77 per cent from the rest of the body.

In animals injected with epinephrin all the glycogen which disappeared was derived from the body, the glycogen of the liver being actually increased. After insulin, 43 per cent of the disappearing glycogen was derived from the liver and 57 per cent from the body. The differences in carbohydrate oxidation were extreme and point to the great differences in action on carbohydrate of epinephrin and insulin. In comparison with the controls, epinephrin injection caused an increase in carbohydrate oxidation of 19.5 per cent and insulin, 97.3 per cent.

The so-called antagonistic effects of epinephrin and insulin on sugar metabolism are, in the light of the Coris' work, not antagonistic in the sense that one opposes the action of the other, for it will be shown later in this article that insulin very likely counteracts the action of epinephrin by synthesizing the precursor of glycogen which epinephrin breaks down. Cori and Cori, however, state that, "Whether or not these two hormones act antagonistically by influencing the same process in an opposite direction must remain undecided as long as the actual point of attack on the carbohydrate molecule is unknown. . . . ." "Insulin is the hormone that leads to a preferential utilization of blood sugar and indirectly of liver glycogen. The antagonistic action between insulin and epinephrine is explained by their divergent effect in blood sugar utilization."

Macleod (6) had predicted the same thing without the experimental facts later demonstrated. "Although in their effects on blood sugar, the two hormones may therefore be said to be antagonistic, it must be remembered that this may be of little physiological significance, and merely be due to the fact that insulin leads to the disappearance from the blood of the excess of glucose which epinephrin causes to be liberated from the liver just as it does when the excess of glucose is absorbed from the intestine, or administered parenterally."

It has now been shown that epinephrin actually acts on muscle glycogen and that the increase in the blood sugar is due to the formation of liver glycogen from the lactic acid derived from muscle glycogen. Blood sugar rises because the increased liver glycogen gives some additional sugar to the blood and this accumulates due to a depression of utilization by the peripheral tissues. The blood sugar is again available for use in oxidations and in storage of glycogen in the muscles and the cycle is complete.

This "cycle of carbohydrates" with lactic acid in the intermediary stage is based upon some of the soundest physiological research. A. V. Hill (7) has outlined series of changes taking place in muscle which his own researches and those of Meyerhoff and Fletcher and Hopkins have established. These changes studied in the complete absence of oxygen are as follows:

"(A) Glycogen disappears.

"(B) Lactic acid appears in equivalent amount.

"(C) Preformed CO_2 is driven off.

"(D) Heat is produced proportional to the lactic acid formed.

"(E) The hydrogen ion concentration rises."

The part played by the lactic acid has been described. Hill says that in the period of recovery (following the anaerobic phase above) oxygen must be taken in to provide the necessary energy. He describes the two phases in the recovery process. The first is the oxidative removal of lactic acid in the muscles where it was formed, and the second is the removal of lactic acid which has

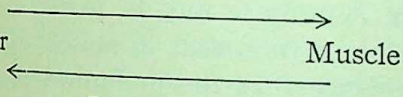
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...ance to escape by diffusion into the blood. It is this part which escapes oxidation (with the consequent liberation of energy) that Cori and Cori describe as the precursor of liver glycogen and a link in the "carbohydrate cycle." These findings (in so far as epinephrin causes a decrease in muscle glycogen and an increase in liver glycogen) have recently been corroborated by Blatherwick and Sahyun (8) and by Himwich, Koskoff and Nahum (9) who also demonstrated the part played by lactic acid.

"The glucose and lactic acid content of the blood of twenty-nine amytalized and eleven decerebrate dogs was studied during rest and exercise. As indicated in the schema, a glucose-lactic acid cycle exists between muscle and liver. Lactic acid liberated from muscle finds its way to the liver through the blood stream, and is there converted to carbohydrate. The liver in turn yields glucose to the blood, thus affording a supply of carbohydrate to muscle.

Glucose



Liver Muscle

Lactic acid

It must therefore become apparent that by virtue of this cycle, the liver becomes an integral part of the mechanism of recovery."

The part played by insulin seems in most respects opposed to that of epinephrin. Insulin acts by utilization of liver glycogen instead of muscle glycogen. It increases the peripheral oxidation of blood sugar as well as converts it into an unknown storage substance. In bringing about these effects it causes the withdrawal of liver glycogen which is converted into blood sugar. Liver glycogen is the only source of blood sugar and insulin acts both in the phase of liberation of glycogen and in the phase of utilization of the liberated dextrose.

In considering the action of insulin it becomes more apparent that glycogen is not a mere storage form of sugar but is in all probability an indispensable intermediary stage in the final utilization of carbohydrate in the body. Irrespective of its origin either from carbohydrate or protein (or possibly fats), it must finally be deposited in the liver to be available for formation of blood sugar. It has been suggested that this may be a necessary step because the dextrose which is formed from liver glycogen may be of a different type from the α-β-dextrose from which it is synthesized. In view of the unavailability of muscle glycogen it is possible that the glycogen synthesized in the liver is also of a different type than muscle glycogen. Glycogen is not well understood in its chemical characteristics. The evidence of a special form of "active" dextrose differing from α-β-glucose, which may be necessary before it can be oxidized by the body has been given in previous issues of the JOURNAL. Insulin may either be necessary for the formation of this special type of dextrose which can then be oxidized by the tissues, or it may require it, and no other type, in order to effect the oxidation. Another possibility may be suggested. Insulin may be necessary for the formation of a special type of glucose capable of being synthesized into the unknown substance (hexose phosphate?) which is a precursor of glycogen. The mechanism of action of insulin, however, on glycogen formation and sugar utilization is not understood. In diabetic animals insulin injections cause a disappearance of sugar from the blood by increased oxidation and an increased formation of glycogen. In normal (starved) animals, however, insulin inhibits glycogen storage, and in normal well fed animals it reduces glycogen. Macleod says that in normal animals the amount of free glucose in the tissues (tension of glucose) is reduced and sugar disappears from the blood: this disappearance is not due to a polymerization of glucose to glycogen or entirely to an increase in the relative amount of carbohydrate undergoing combustion. Macleod terms the condition which permits the relatively

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enormous removal of sugar from the blood, a "sugar vacuum" of the tissues. Experimental evidence is against the conclusion that the sugar disappears as a result of some sort of glycolysis in the blood itself, whereby the blood simply holds the products of sugar hydrolysis. Actually the experiments showed that the site of insulin action is in the cardiac and skeletal muscles and not in the liver. Since in normal animals the removal of sugar by insulin can not be accounted for by increased formation of glycogen or entirely by increased oxidation, the problem becomes one of accounting for the fate of the sugar. Macleod (9) accounts for it as follows:

"We believe by assuming that insulin stimulates the formation of some unknown substance which maintains a certain equilibrium with glycogen, and stands on the way between this and lactic acid. This unknown substance may be a stepping stone in the conversion of carbohydrates into fats, and it is possible that in its formation a phosphorous acid complex, such as hexose phosphate is involved."

In addition to this storage of blood sugar as glycogen or as an unidentified precursor of glycogen, there is an increased oxidation of carbohydrate following insulin injection. This is shown by an increased respiratory quotient and by an increased oxygen consumption. The extent to which it is oxidized, however, can not account for all the sugar leaving the blood. In diabetic animals the action of insulin is to definitely increase the oxidation of carbohydrates.

The possibility of some endocrine substance or substances secreted by the pancreas, other than insulin which might exert an influence on carbohydrate metabolism has long been a subject of speculation. Many experiments and clinical observations strongly suggest it. N. F. Fisher (10) reached the conclusion that "Insulin probably does not represent the entire pancreas hormone complex, since in the total absence of the pancreas insulin can not maintain life or does not control all the diabetic symptoms (subnorm weight, polyphagia, polyuria)."

Chaikoff, Macleod and Markowitz found that when insulin injections were supplemented by daily feeding with raw pancreas, dogs could be maintained in good bodily nutrition and concluded:

"That the presence of something derived from the pancreas either its digestive ferments or some internal secretion besides insulin is necessary for the maintenance of normal metabolism."

Recently, Ronzoni, Glaser and Barr (1) have demonstrated the presence in the pancreas of a substance which exerts an inhibitory effect on glycolysis in muscle. They also arrive at the conclusion that a hexose phosphate (see Macleod's assumption above) is a necessary part of lactic acid formation in muscle. "In muscle extracts then the chief mechanism by which lactic acid is produced is through the intermediary involving carbohydrate and phosphate disappearance, presumably hexosephosphate. Unless the mechanism existing in muscle, frozen and hashed is different from that in muscle extract, there is evidence that the preformed precursor of lactic acid existing in muscle is a complex involving carbohydrate and phosphate." This work suggests that (at least in solution in muscle extracts) carbohydrate combines with phosphate to form hexose phosphate and this compound is then broken down into lactic acid and phosphate. The inhibitor element of the pancreas acts on the phase of phosphate-carbohydrate formation—inhibiting the process of esterification and preventing an accumulation of this precursor of lactic acid. The subsequent breakdown of the ester (hexose phosphate) into phosphate and lactic acid is not materially affected by the inhibiting substance.

The knowledge of the opposed effects of pancreas internal secretion and epinephrin on blood sugar has been largely extended. The following facts have apparently been demonstrated. Both exert their action in

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peripheral tissues and not in the liver or on sugar in the blood. Insulin apparently stimulates the production of an ester or some unknown substance (probably hexose phosphate) and a pancreatic inhibitor substance retards it. This substance (hexose phosphate?) is a precursor of glycogen and doubtless stands in chemical equilibrium with it. A pancreatic inhibitor substance exerts an opposed effect and inhibits the synthesis of hexose phosphate. Epinephrin increases the mobilization (oxidation) of muscle glycogen and decreases the utilization by the muscles of blood sugar. The products of muscle glycogen splitting (lactic acid) are synthesized into liver glycogen.

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A Contribution to Kottmann's Reaction

(Translated from the article by Dr. Emil Walder, *Mitt. Grenzgeb. Med. u. Chir.*, 1926, 39 : 626, No. 4/5.)

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(CONTINUED FROM VOL. XIV, NO. 2)

III. *Concluding Remarks*

In the work given before we have regarded the Kottmann reaction perhaps too much from the standpoint of pure colloid chemistry; in this we are, however, convinced that the colloid chemist himself would have proceeded still more critically. We drew attention to positive sources of error of the method and showed that the opinion of Kottmann that the degree of browning of his sera is a direct measure for its degree of dispersion or its dispersibility is not yet demonstrated, which moreover Prof. Kottmann acquiesced in an oral discussion. We showed that the relations between degree of dispersion and degree of browning are not of so simple a nature, and demonstrated in concrete examples, as Kottmann himself also says, that "profound investigations are still necessary to clear up the theoretical basis of the method in all directions" or, as it is reported later, "that without doubt the method is still further to be cleared up and in need of development in various points".

If we review the literature which has appeared concerning the Kottmann reaction, we must observe that certain authors who work with the method, perceive in it, as it were, a dispersometer for serum and in part on the basis of their results with the Kottmann reaction produced theories concerning physiology and pathology of the thyroid

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function, which, it appears to us, go somewhat too far. So, for example, says F. Starlinger ("Physico-Chemical Investigations on the Thyroid Problem," *Grenzgeb.*, Bd. 36): "And finally Kottmann offered his photoreaction, which properly first conceived the physical condition of the albumin colloid in the serum, so to speak, bodily . . .." That this physical conception of the albumin substance is still problematic we believe we have shown sufficiently. We do not wish to enter into this point, but permit ourselves several remarks on another declaration of Starlinger. In the same work, Starlinger says, in part on the basis of his results with the Kottmann reaction, that a task of the thyroid is to transform coarsely disperse albumin into finely disperse. A struma which does this is said to be hyperfunctional; on the other hand, the reverse is also said to occur, that, to be sure less frequently, the finely disperse serum appearing in the thyroid leaves it as coarsely disperse, "lowering of the plasma dispersion in venous blood characterizes the hypofunctioning goiter." A positive contradiction appears to us to be present here. A gland, which reverses its function on the contrary — which was the case in the hypofunctional struma, according to what was said above — does not seem to us to be hyperfunctional; in our opinion, it should rather be called "contrafunctional." That in general a gland can reverse its function to the opposite, seems explainable with difficulty. It is well known that there are ferments which reverse their effect from a certain concentration of the reaction product. That, however, a whole gland reverses its activity, falls out of the bounds of what is known up to the present. A gland can show hyper-, dys- or hypofunction. We do not, however, as yet know "contrafunction." If the normal or hyperfunctioning thyroid truly displays a dispersing activity for the serum, it must be assumed that the diseased, hypofunctioning gland does this in lessened measure or no longer at all. The border case would therefore be that in which the gland simply allows the blood to pass through changed, so that the entering and leaving plasma shows the same dispersion. One could only arrive at the Starlinger conception if one would make the auxiliary hypothesis that the dispersion would be coarsened by passage through any indifferent organ. Points of support for such an assumption are however not known to us. The difficulty with the whole thing must lie elsewhere. Before we can proceed with the solution of such questions, we must have at our disposal methods which permit us to compare the degree of dispersion of the various sera or plasma, measured in absolute proportion, free from objection. This is, however, not yet the case. Aside from this we do not in general know how the physical process of change of dispersion stands in respect to the chemical decomposition of the albumin molecule which seems to stand in the foreground in thyroid function. Increase in dispersion proves no albumin decomposition as yet, although it can precede it. It is self evident that nothing is changed in the fundamental question of an internal secretory process in the thyroid through these discussions concerning the dispersion.

As far as the method is concerned, Starlinger also says that the values of the Kottmann reaction are of course to be realized with some precaution, since precisely with this method the individual shades of color present a rightly subjective factor. He prevents the coagulation of the blood through the addition of citrate, in order to be able to determine the dispersion of the plasma; now we have already cited at the beginning of our work the changes in color observed by Lippo-Cramer in the growth of gelatin-containing silver germs under the influence of phosphate or citrate. The possibility is suggested that also in the colloid silver arising according to Kottmann, the color changes may appear under the influence of citrate. One would accordingly first have to test the influence

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of the citrate experimentally. Whether the citrate is without influence on the dispersion of plasma we also do not know.

Still another brief remark on Starlinger's work. He says that the cubital vein blood serum on which the whole organism has finished working can not give any more enlightenment concerning the function of the thyroid. Of course, the thyroid secretion is very quickly changed in the living blood or organism as the most recent investigations show. The investigations of Hara and Branovacky show, however, that in pronounced functional disturbances it still remains biologically active. Our own investigations show the same thing. In our tables we also compare with each other venous blood sera from the arm in normal, exophthalmic goiter patients and cretins, in order to determine that in exophthalmic goiter the delay in reaction is definite and the degree of browning is a little less intensive. Moreover, Kottmann's investigations show this already, and he performed his reactions only with venous blood from the arm.

Another author, E. O. Schmidt ("Concerning Morbus Basedowi," *Grenzgeb.*, Bd. 33, 1921) used for the performance of the Kottmann reaction 5 per cent instead of 0.5 per cent solutions of potassium iodide and silver nitrate, subjected it to light with 200 candles for 10 to 25 minutes — at what distance he does not say. In this tenfold stronger concentration of the reagent probably the albuminous substances of the serum, in their function of dispersing agent, result in the ensuing colloidal silver iodide, and the silver is so strong in the background that quite possibly one sees a reaction totally differing from the Kottmann reaction. In so strong a concentration it is possible that most of the silver iodide formed does not remain as a colloidal solution, but instead precipitates out directly. Moreover, we have also referred to the fact that the result of the reaction is in high degree dependent on the amount of light which hits on every square centimeter surface of the reaction mixture; constance of light source, of distance of it from test tube and the time of lighting are, accordingly, absolutely indispensable in order to obtain reliable results comparable with one another. Schmidt has apparently had too little regard for these factors, for his results to be comparable with ours.

With this we have arrived at the conclusion and hope despite the criticism which we had to exercise on the Kottmann reaction — a criticism which does not refer to the clever basic idea of Kottmann concerning the realizability of which we have moreover no doubt, but refers to the present form of practical execution of his reaction and its significance — that we have shown that Kottmann has nevertheless through his method of serological thyroid examination shown a way which when once developed further, can bring valuable results to maturity.

Summary

1. The Kottmann reaction in the form described here for its practical execution, in so far as this may be judged from the cases investigated here, gives results in the sense that the sera developed according to it stain brown in varyingly marked degree; the most pronounced degree of browning is shown by the dwarf cretin sera; the weakest by the exophthalmic goiter sera; in between lie the sera of goitrous cretins, of ordinary goiters and the normal sera. The goiter venous blood sera show in general less marked degree of browning than the venous blood sera from the arm. The degree of brown coloration may be related more or less well (with several exceptions) with the clinical picture of the case in question.

2. If we disregard dwarf cretin sera and severe cases of exophthalmic goiter, the differences in degree of browning between the individual maximal developed sera are not very great.

3. These degrees of browning were measured on a Kollargol standard which remained constant for this.

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4. Concerning the relation between degree of dispersion and degree of browning there are not as yet any experimental investigations; Kottmann's opinion that the browner a serum developed by his method is, the more coarsely disperse its micelles, is accordingly not proved. The conditions seem to be quite complicated here.

5. Essential sources of error are connected with the Kottmann reaction, which are conditioned by the capriciousness of the silver iodide and of the colloid silver, with respect to their color and degree of dispersion.

6. The sequence of addition of the agents, the type of light, are of great influence on the result of the reaction; a constant technique strictly adhered to in experiments is accordingly an unconditional requirement in the execution of the reaction.

Practical Therapeutics

High Blood Pressure

THE intense interest displayed in recent years by profession and laity in high blood pressure is not of itself evidence that this condition is more frequent than formerly. The development of the clinical sphygmomanometer with the consequent ease in estimating blood pressure, the increased publicity given to life insurance and public health and mortality records, have all served to fix attention on this rather widespread condition of pathological physiology.

Hypertension is doubtless a precursor of arteriosclerosis and of general cardio-vascular disease but it is frequently, perhaps usually, found unassociated with these conditions. When associated with arteriosclerosis, however, the term "essential" hypertension is commonly applied.

The symptoms of arteriosclerosis, therefore, are chiefly the symptoms of the hypertension.

Toxic conditions have received much attention as a cause of hypertension and of arteriosclerosis, and it seems likely that a common toxic factor is the cause of both. Foci of infection, teeth, tonsils, chronic appendix, etc., metabolic diseases giving rise to toxic products of metabolism, have been related to both the arterial hypertension and the arterial changes. Obesity and diabetes likewise seem causative and suggest a toxic factor. Hartman and Ghrist (1), in a study of 2,611 cases taken from the records of the Mayo Clinic, found, "The inconstancy of the diastolic readings emphasizes only the striking constancy of increase of systolic blood pressure with increasing weight in a non-selected group of office patients in a general practice."

In an exceedingly enlightening paper, Blackford, Bowers and Baker (2) have shown the strong family tendency of this condition, its incidence after 50 years of age and its tendency to persist. They have analyzed the histories of 222 of 401 patients who were examined from 5 to 11 years ago. Their conclusions are:

"A study of 401 hypertensive patients (systolic pressure 175 or over) found in 10,000 clinical examinations made in a general clinic from five to eleven and one-half years ago has shown that:

"1. The appreciable incidence (1.2 per cent) of hypertension begins in the fourth decade; 5.8 per cent of all patients examined in the fifth decade showed hypertension, 12.3 per cent in the sixth, 22.5 per cent in the seventh, 14 per cent in the eighth, and 10 per cent in the ninth showed blood pressures above 175.

"2. Sixty-five per cent of the hyperten-

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sive cases in this series are in women; 50 per cent of all patients examined were women.

"3. The remarkably greater number of women having hypertension, as compared with men, comes in the fifth, sixth, and seventh decades.

"4. Family histories of hypertension were noted in more than one third of all histories.

"5. Cases of hypertensive disease complicated by goiter, syphilis, diabetes, chronic nephritis and valvular heart disease have each shown by groups no particular difference from cases of pure hypertension.

"A follow-up study of 222 of 401 hypertensive patients (55 per cent) examined from five to eleven and one-half years ago has been made. Twenty of these have been discarded for statistical study because they were moribund at the time of examination or died shortly afterward from other diseases. The 202 cases remaining, followed from five to eleven and one-half years, have shown:

"1. A gross mortality of 50 per cent, a male mortality of 70 per cent and a female mortality of 39 per cent.

"2. A mortality about the same for moderate and marked cases, but twice as high in extreme cases.

"3. An average duration of life after the first observation of thirty-two months for males and forty-four months for females.

"4. An average time since the first examination of 101 living patients of eighty-one months.

"5. Known causes of death, thirty-one from cerebral complications, twenty-five from heart disease, eighteen from uremia.

"We have not found any tendency toward recovery in hypertension.

"Occasionally remarkable exceptions are seen to the general rule of mortality. Women with hypertension sometimes outlive their expectancy. Men almost never do."

The treatment of hypertension falls under the general headings of hygiene, dietary and drug. O'Hare (3) says, "The care of such a patient should be based primarily on the knowledge that the problem is that of a generalized circulatory disorder consisting essentially of a functional vaso-constriction at first, then a more or less progressive small blood vessel sclerosis with superimposed vaso-constrictions, and finally as a result of cutting down of the blood supply to various organs, secondary degeneration and impaired function of these organs."

Rest, freedom from heavy muscular exertion, warm baths, mud baths, light treatment and the cultivation of habits of repose and efforts to relieve a tendency to worry are valuable. Excessive expenditure of nervous and physical energy should be guarded against. Diet, as a rule, is simply arranged by reducing the intake of food down to the energy requirement of the patient. In the overweight patient, reduction of diet and restriction of carbohydrates and fats are important.

For drug treatment, sodium and potassium iodide is classic. In cases with a history of syphilis they are valuable. Amyl nitrite by inhalation is valuable in controlling the sudden increases of pressure so frequently encountered. Nitro glycerin U. S. P. 1 minim by absorption from the mouth is to be used for the same purpose. Potassium sulphocyanate and bismuth subnitrate have recently received attention.

"Chemically pure potassium sulphocyanate was prescribed in a simple aqueous solution of such strength that 1 fluiddrachm (4 cc.) contains 1½ grains (0.1 gm.) of the salt. This dose was given in water by mouth three times daily, after meals, for the first week, twice daily for the second week and thence once daily for the third week of treatment. Thereafter this dose was given daily, or every other day." (4)

Bromides and luminal are most helpful in some cases characterized by nervous irritability. The effect of bismuth subnitrate on hypertension has been carefuliy studied by Stieglitz (5) who suggests the probable mech-

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The Doctor's Page



ARTHUR HARTMANN

(1849-)

The opportunity is not given to every one to serve his country in two wars and in a long interim between, to devote himself to successful private occupation so commendable as to obtain for him the highest honor of his state. In this respect Arthur Hartmann is unique.

He was born on January 1, 1849, in Heidelheim, a city situated near the eastern borde

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of Württemberg. His early life was uneventful. In Heidenheim and later in Stuttgart he received elementary and intermediate education, and at the age of 18 he sought entrance to the University of Tübingen for the purpose of studying medicine. After a little more than two years here his studies were interrupted by the war of 1870-1871, for he entered the military service as assistant physician in the Third Württemberg Field Hospital.

After the war Hartmann resumed studies at Freiburg and then at Leipzig, and in 1873 he was graduated from Leipzig. A brief activity as army physician occupied him until he undertook a journey to England, where he became acquainted with Lister, and to France. The years 1875 and 1876 Hartmann spent in Vienna studying especially diseases of the ear, nose and throat and after this extended period of preparation, in which he availed himself of much practical application he ventured definitely to set himself up as a doctor of diseases of the ear, nose and throat in Berlin (1876). The fact that he was found still practicing in Berlin 35 years later is meritorious. Excellent training in his subject and accurate diagnosis of the material presented soon won for Hartmann a reputation, not only in Germany but in other countries as well.

In order to satisfy an inclination to teach, Hartmann founded a polyclinic, where, from 1881 to 1894 he gave courses in his special subject. These lectures and classes were attended by physicians from all parts of the globe, who were desirous of acquiring the excellent technique of this man and of benefiting from the profound researches he carried on. In 1902 the title of Professor was bestowed upon him, in honor of his distinguished service. When the Rudolf Virchow Hospital was founded in 1905, Hartmann was called to the post of directing physician of the department of Diseases of the Ear, Nose and Throat. In 1909, his honorary titles culminated with that of *Geheimer Sanitätsrat*, the highest he could achieve. The following two years were crowded with much activity in his special field, and then he settled down for a well earned rest in his native city, Heidenheim. He turned his attention to social service, becoming the Director of the Society for the improvement of Heidenheim; as an outgrowth of an interest in Uhland, he published a popular book referring to this locality and held a very successful exhibition of Uhland material in Tübingen. He was also identified with activities intending to curb the use and sale of alcoholic beverages in his province.

It was not long, however, before the tranquillity of his life was interrupted by the World War. He again entered the service of his country in medical capacity. In the early part of the conflict he was head physician in a hospital train, and later, though he had already led an active life passed his 65th year, he took charge of a reserve hospital until the end of the war.

Hartmann has contributed a great deal to the service of mankind, in his practice by the judicious application of knowledge gained from accurate pathological, anatomical and clinical investigations and by recording his findings in numerous scientific publications. Many of his writings, of which the greater part is composed of books or monographs, deal with diseases of the ear, nose and throat, and especially with deafness and dumbness and the education of the deaf and the dumb. Some of these are *Experimental Studies on the Function of the Eustachian Tubes* (1879), *Deaf-dumbness and the Education of the Deaf and Dumb* (1880), *Diseases of the Ear and Their Treatment* (1881) The success and reliability of the last two books have been so great as to more than justify their republication and translation from German into other languages. *Atlas on the Anatomy of the Frontal Sinus* (1900), *Textbook for the Instruction of the Deaf* (1909), *The Deaf Individual in the School* and *The Education of the Totally Deaf in Germany* (1912) render evidence that Hartmann not only treated his patients but also followed up with more permanent aid to those particularly afflicted with the handicaps of deafness and dumbness.

Hartmann broadened the scope of his literary activity when he took charge of the publication of *Zeitschrift für Ohrenheilkunde* after the death of Professor Moos. For a number of years the *Vierteljahresbericht* prospered under his expert supervision. From 1900 to 1904 he edited the *Verhandlungen der Deutschen Otologischen Gesellschaft* and became its President in 1906. Recently Hartmann has been attracted to the subject of nutrition and published, in 1928, a volume on *Nutrition and Raw Diet.*

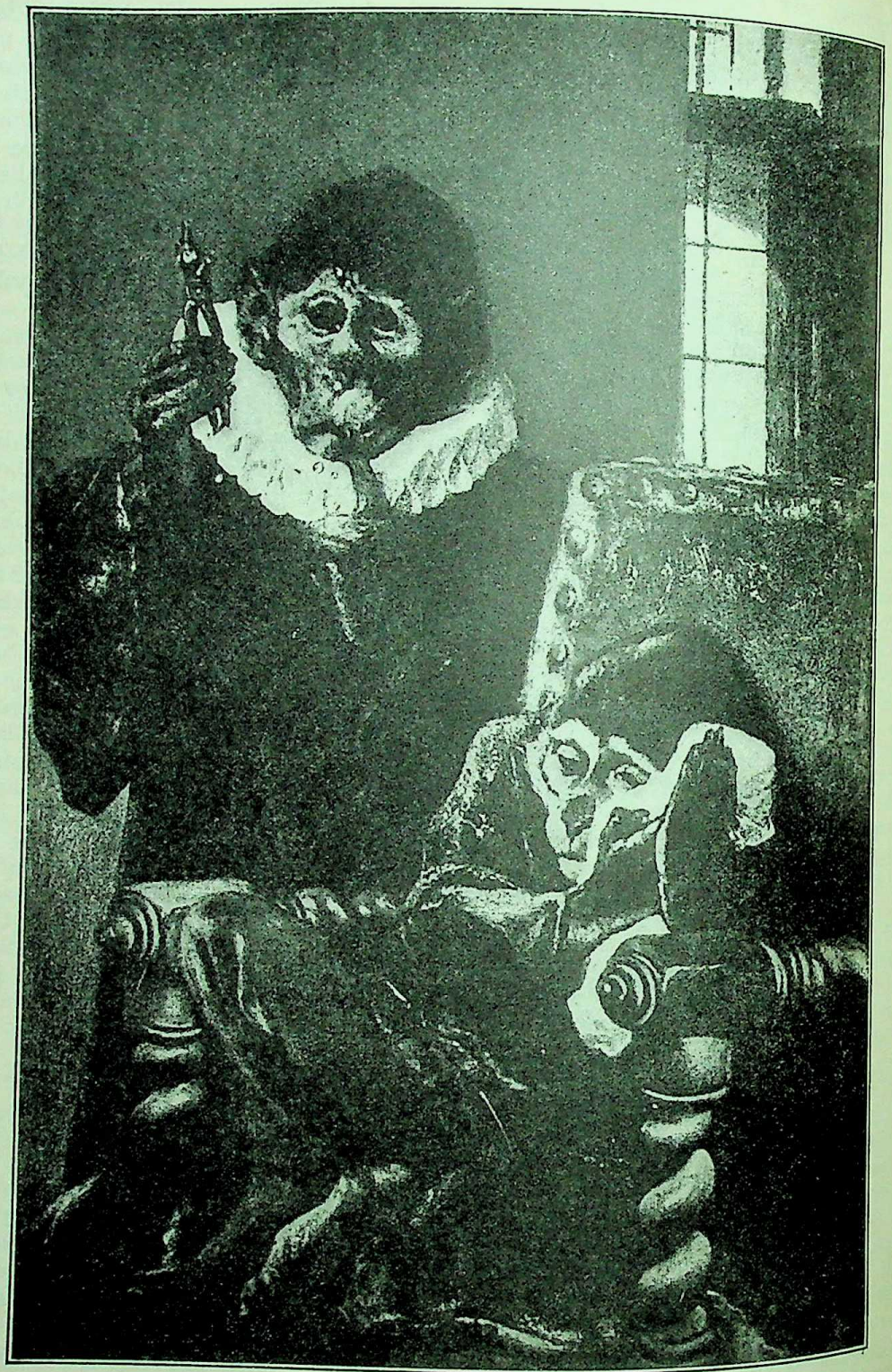
During his active scientific career Professor Hartmann was interested in all things medical

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Medical Subjects by Famous Masters



"THE MONKEY DENTIST," by Michel Marie Charles Verlat (1824-1890)
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Editorial Comment

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Crystalline Ovarian Hormone

SINCE the preparation by Allen and Doisy of solutions containing the active estrus-producing hormone of the ovary, the activity of which was demonstrated by the vaginal smear method, there has been widespread activity in attempts to isolate the hormone as a pure crystalline substance. It is true that active extracts had been prepared before Allen and Doisy but they were of uncertain strength; the methods of preparation were complex and uncertain and there was no way of standardizing them or of comparing their values. The "lipoid" character of the ovarian hormone was first demonstrated by Iscovesco and his 11 Fb and V Dc, soluble in ether and alcohol, were among the best known preparations 15 years ago.

Seitz, Wintz and Fingerhut, Aschner, Frank, Rogers, Fellner, Herrmann and others made extracts of varying activity in the early period of study. The method of assay was more in the nature of a qualitative test — the effect on hypertrophy of uterus and tubes, on animal behavior, etc.

The introduction by Allen and Doisy of the Papanicolau-Stockard method of determining estrus by the vaginal smear method in 1923, made precise valuation possible and contributed enormously to all succeeding research.

The oily (lipoid) character of these preparations was a decided disadvantage and necessitated either the use of a bland inert oil for injection or the use of a colloidal aqueous solution.

Further research made clear, however, that although the active principle was extracted with lipoid solvents and was apparently itself a lipoid, it was possible to split the hormone from the oil and make a true water solution. Zondek, Laquer, Dickens and Dodd have been able to prepare these water-soluble preparations.

The estrus-producing hormone (as distinguished from the inhibiting hormone of the corpus luteum) may be obtained from the liquor folliculi of the ovary, from the placenta, from the blood, and from the urine of pregnant women.

Very recently Doisy, Veler and Thayer (1) have prepared the hormone in crystalline form.

"A crystalline product which has been recrystallized several times has been isolated from the urine. The assays show that the crystals are physiologically more active than any preparation obtained thus far, the activity being more than 2000 rat units per milligram."

This work of Doisy and his associates confirms the opinion of others that the principle obtained from liquor folliculi and the urine is the same. In the *Lancet* of January 4, 1930, it is reported that Dr. Butenandt of Göttingen has also produced a crystalline ovarian hormone.

"Butenandt worked with an oily material which was obtained from the urine of pregnant women, and contained about 30,000

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mouse-units per gramme. By repeated distribution between two solvents (aqueous alcohol and petroleum ether) inactive substances were removed in the petroleum ether fraction, and the material then had 500,000 mouse-units per gramme. This substance was further purified by the use of other solvents (ether, benzene, and ethyl acetate) and by adding alkali in increasing strength to the acid solution. An alkali-soluble fraction was obtained which had a mouse-unit of only 1.5 to 2 millionths of a gramme. Further purification was effected by distilling this oil in a vacuum of 0.20 — 0.03 mm. Hg and at a temperature of 130 — 150° C., and the material then contained 5,000,000 units per gramme. Sublimation in a high vacuum or treatment with solvents yields a crystalline product of which one gramme contains 8,000,000 mouse-units.

The development of a crystalline hormone of such astonishing potency is interesting in view of the lack of effects found by Frank at Mount Sinai Hospital, New York, in the case of practically all of the best known commercial products of a "purified" and "concentrated" estrous hormone.

The field of application in practical medicine of such a product is not yet demonstrated. Novak has pointed out the fundamental biological differences between estrus in lower animals and menstruation in the human female. Evolution has changed the process and altered the values of the several elements active in producing menstruation. In the human female the usual menstrual mechanism is greatly dependent upon the corpus luteum although the follicular hormone is, of course, important. Some cases may be observed in women in which there is a persistence of the more primitive follicular type of menstruation, but in general, human menstruation is not solely dependent upon the follicular hormone and it is not to be expected that this hormone alone will suffice in the treatment of irregularities of menstruation.

1. Doisy, E. A., Veler, C. D., and Thayer, S., *Am. J. Physiol., Abst.*, 1929, xc, 329.

Abstracts

The Ovarian Hormone and Its Site of Development. — W. Lahm. (*Zeitschr. ärztl. Fortbild.*, **26** : 78, 1929.)

The ovary accelerates ossification, controls sexual life, hair and growth of beard, development of baldness, pigment metabolism, tonus of the blood vessels, metabolism in the capsular ligaments (arthritis ovaripriva). Primary agenitalism is combined with hypotonia. In the climacteric the ovarian deficiency causes hypertonia. The generative function might also be the object of certain internal secretory relations. The most recent experimental investigations favor the idea that the disintegration of the ova and their resorption excite vegetative impulse. The substances which induce the growth impulse in the uterus — ovarian hormone — were originally obtained from the ovary. Today we know that numerous albumin substances, histamin, etc., can exert a growth stimulus on the uterus. The following requirements were set for the ovarian hormone: lipoid solubility, indestructibility (indestructibility even through digestion), specific activity, preparation from ovary, placenta, blood or urine.

Hypoglycemic Action of Combined Borate and Insulin. — Loeper, Ravier and Tonnet. (*Progrès méd.*, **47** : 189, 1929.)

The authors undertook experiments on four diabetic patients. Their blood sugar varied from 2 gm. to 3.50 gm. The patients first received injections of pure insulin; to the second injection, 0.45 or 0.90 sodium borate was added. In two cases the strengthening of the insulin effect and the reduction of sugar excretion through the combination with sodium borate were evident. In one case the inverse effect occurred: the combined injection had less of an effect than pure insulin injection.

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Concerning the Hormonal Therapy of Ovarian Hemorrhages. — Kraul. (*Wien. klin. Wochenschr.*, 42 : 158, 1929.)

Demonstration of a series of youthful patients in whom transfusions of 100 to 150 cc. of blood of pregnant women were undertaken on account of profuse, irregular hemorrhages, after styptics, curettements and irradiation of the spleen had remained without effect. Kraul considers the action of injections of blood of pregnant women to be the result of the hormone content of the pregnant blood, in favor of which the lasting success of the treatment also speaks.

Hypogenitalism. — Serdukoff. (*Progrès méd.*, 21 : 901, May 25, 1929.)

By hypogenitalism is meant the various endocrine disorders intimately connected with decrease, disappearance or absence of the genital glands. In women, the period of puberty and that of the menopause may be regarded as the manifestations of a physiological hypogenitalism; just as there are endocrinopathies with distinctly pathological tendency such as chlorosis and eunuchoidism.

Chlorosis is one of the affections observed exclusively in girls at the time of pubertal development. This condition is intimately connected with the decrease in internal secretion of the ovaries or with the delay in formation of the endocrine products of these glands. The greater number of symptoms of chlorosis indicates hyposecretion; certain ones may be explained as being the result of an autointoxication due to dysfunction of the endocrine glands. Chlorosis is regarded as a pluriglandular affection: in addition to the ovaries, the thyroid and pituitary are also involved.

In the amenorrheic forms of chlorosis good results of treatment are obtained by different organotherapeutic preparations extracted from ovarian substance, especially in combination with iron. In the menorrhagic forms it is logical to prescribe preparations of pituitary. In general medical treatment should be associated with regulation of living conditions and principles of general hygiene to aid the organism in the critical time of puberty.

Individuals are designated as eunuchoids who give the impression of castrates, even though their genital glands have not been extirpated. The genital insufficiency to which the various forms of eunuchoidism are related may present a symptom complex identical to that arising after complete ablation of the genital glands. Congenital or natural eunuchoidism is the result of congenital aplasia of the sexual glands; there are also atypical forms of eunuchoidism. From the clinical viewpoint in women totally castrated a characteristic symptom complex develops: menstruation is arrested. Later there appears atrophy of the mammary glands, of the external genital organs and of the uterus. There is retardation of development of the bones of the pelvis and of the lower extremities in the castrated woman. General appearance changes and the patients acquire masculine traits. Then, as result of the lack of endocrine influence of the ovaries, vasomotor, secretory, emotional and psychic disorders develop. There is also observed disturbance of general metabolism. The post-operative disorders are not so manifest after castration of mature women. Congenital eunuchoidism is rare. The symptoms of eunuchoidism correspond to those observed in castrated women: osseous modifications as well as absence or total disappearance of hair; menstruation is missing in typical cases; sexual desire is wanting.

Eunuchoidism is intimately related to deficiency of function of the genital glands. Among the number of etiological causes there is admitted emotional shock during intrauterine life. Traumatisms, infections and septic affections with destruction of the parenchyma of the genital glands may be related among the principal etiological causes of the late secondary forms of eunuchoid degeneration.

The differential diagnosis of eunuchoidism does not present any great difficulties in typical cases with definite symptom complex. The results of treatment are variable according to whether ovarian tissue capable of functioning is present or not. Most frequently treatment is symptomatic. Organotherapy may be applied by mouth or in injections; various ovarian preparations being used. In general, injections are most recommended. In certain cases of hypogenitalism and in particular in certain forms of hypoövarianism and eunuchoidism, there is noted decrease in sexual desire. In these cases associated treatment (ovarian preparations and yohimbin) is recommended. In cases where the symptoms of hypogenitalism are especially marked in the osseous system, it is good to apply combined treatment with ovary and calcium. In cases where primary lesions

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of the genital glands are associated with pluriglandular disturbances, treatment with thyroid or pituitary must be associated with ovarian treatment.

When eunuchoidism in women is accompanied by obesity, loss of hair and modifications of metabolism with retardation of the process of oxidation good results may be obtained with treatment by minimum or moderate doses of thyroid. In certain cases the symptoms of obesity psychic apathy, intellectual indifference, weakness of memory, muscular fatigue, fall of hair yield to associated treatment with the three principal glands of the organism: ovary, pituitary and thyroid.

In cases of total absence of the genital glands, after castration or in congenital eunuchoidism, the modifications assume so tenacious a character that treatment with simple or complex endocrine preparations remains unsuccessful.

The most real method of treatment at the present time applied to cases of eunuchoidism hypoövarianism and other forms of the hypogenital syndrome is the transplantation of endocrine glands. The transplantation of genital glands in eunuchoidism (homo- or hetero-transplantation) produces a good stimulatory effect. The transplantation often contributes to the arrest of atrophic processes of genital involution in the case of secondary eunuchoidism. In the primary forms of genital eunuchoidism transplantation of the ovaries relieves the painful nervous, vasomotor, psychic and somatic symptoms.

Hyperthyroidism Evolving towards Hypothyroidism in the Course of a Treatment with Iodin. — L. Dautrebande. (*Presse méd.*, **37** : 721, June 1, 1929.)

The author reports a case of a young man of 20 years with goiter and hyperthyroidism which was transformed into hypothyroidism during an iodin treatment. He calls attention to three interesting points in this clinical observation: (1) a definite case of hyperthyroidism may be transformed into hypothyroidism under the influence of iodin. The author observed another case where the metabolism fell from +10 to −11 after 3 weeks of treatment and rose again immediately afterward. With Lemort, he also observed a third case where the hypothyroidism attained −20 per cent but was transient. This is the first time, the author believes, that the appearance of a prolonged hypothyroidism following administration of iodin has been reported. (2) The second interesting point is a change in the exterior appearance and intellectual habitus of the patient during the treatment. This change is paradoxical as the patient observed distinct signs of cretinism disappear at the time when the metabolism had been below normal for several weeks. (3) Finally a third point of this case report is worthy of mention: the coincidence of a definite hyperthyroidism with a soft goiter without nodules appearing clinically as a simple colloid goiter of adolescence and the transformation of this simple hyperthyroid goiter into a hard adenomatous protuberant goiter contemporaneous with a hypothyroidism, whereas this type of hard goiter is frequently the accompaniment of toxic hyperthyroidism.

Clinical examination alone is not sufficient for drawing a conclusion of hyperfunction or hypofunction of a thyroid; determination of the basal metabolism remains the indispensable diagnostic aid.

Further Investigations in the Preparation, Biology and Clinic of Pituitary Anterior Lobe Hormone. — B. Zondek. (*Klin. Wochenschr.*, **8** : 157, 1929.)

The anterior lobe hormone is a very sensitive substance which in contrast to folliculin is destroyed by cooking, acids and alkalis. Whereas folliculin is soluble in ether, anterior lobe hormone is insoluble in the majority of lipoid solvents, so that (for example in the preparation from urine of pregnant women) a separation of the two hormones is possible thereby. In the preparation of the hormone from the pituitary anterior lobe, placenta and pregnant urine, results are least objectionable and the gain is better by the way of precipitation which the author uses for the past 1½ years. It could be determined that pituitary anterior lobe hormone is precipitated under certain conditions through a series of organic solvents miscible with water (for example, ether, alcohol, methyl alcohol, acetone, etc.).

With dissolution of the precipitant in water there remains an insoluble residue which does not contain the hormone, so that in this way also a further purification is possible. The desiccated substance remaining, containing the hormone, is soluble in water.

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The author's investigations were undertaken on sexually mature (1600 to 1800 gm. weight) animals, as well as infantile animals (1100 gm.). Following 10 to 14 days of treatment (2 to 4 cc. pituitary anterior lobe extract equals 60 to 120 rat units *pro die*) there was shown a powerful influence of pituitary anterior lobe extract on the genital apparatus. The uteri had been transformed from thread-like tubes to formations as thick as one's finger (blue-red, livid in color) which contract immediately upon the stimulation of opening of the abdomen. In infantile animals one had the impression of a young pregnancy. The ovaries, of the size of lentils, became almost as large as cherries, replete with blood dots and golden yellow corpora lutea. Sections through the vagina showed less changes of the mucosa, especially increase in thickness of the vaginal musculature. The uterus showed this growth under the action of pituitary anterior lobe in still more pronounced degree. Here especially the markedly polypous proliferated uterine mucosa is conspicuous which is quite similar to a pregnancy mucosa in the rabbit. In the ovary the primordial follicles are displaced on the border zones in consequence of blood-filled luteinized follicle, in which in addition to the granular proliferation, the splendidly developed theca must especially be referred to. In the discussion, Aschheim could demonstrate the isolated, partly luteinized theca proliferation in the mouse under the action of pituitary anterior lobe.

The author knows little concerning the clinical action of pituitary anterior lobe extract in human beings, since he has used it only for the past ¾ year in the clinic.

Clinically the author was able to determine that anterior pituitary intramuscularly injected has a marked hyperemic influence on the female genital apparatus so that a picture of a young pregnancy can be simulated by turgor and color. This action determined through direct contemplation in operations he found corroborated thermometrically. The author was able to determine a rise in temperature of the peritoneum, which lay not as usual at 0.5°, but up to 1° above the axillary temperature. This pelvic hyperemia can doubtless be utilized clinically. Following a suggestion of P. Klein anterior pituitary extract is being used by the author in the University Clinic for Women of Charité, Berlin, in inflammatory pelvic affections in women, in order to induce the therapeutic effect through the hyperemia.

Through pituitary anterior lobe extract a stimulus to ovarian function in women is exerted and through it secondarily on the structure of the uterine mucosa. If one injects pituitary anterior lobe extract from the first day of menstruation to the eighth day of the cycle and then examines the uterine mucosa, a structural stage is found in this, which corresponds to about the 14th to 16th day of the cycle, the beginning of the secretion phase.

Concerning the Influence of Thyroxin on the Metabolism of Surviving Tissue. — K. J. Anselmino, O. Eichler and H. Schlossmann. (*Biochem. Zeitschr.*, **205** : 481, 1929.)

The reports in the literature concerning the action of thyroid hormone on respiration and fermentation of surviving cells are contradictory. The results of experiments which the authors carried out showed as the most striking change the increase of anaerobic glycolysis of the kidneys.

In sections of spleen, liver and kidneys of white rats 24 hours to 7 days following injection of thyroxin only a very slight or no increase in respiration was found, measured by means of Warburg's method. The anaerobic glycolysis of the kidney increases all the higher the stronger the increase of consumption of oxygen effect in the living animal through the thyroxin. The anaerobic glycolysis of the liver and spleen is not increased. The experiments prove that the thyroid hormone attacks the anaerobic phase of the metabolism in the first place.

On the Female Sex Hormone. III. Contribution. The Activity of the Estrous Hormone by Oral Administration. — F. Lange and W. Faure. (*Deut. med. Wochenschr.*, **52** : 310, 1926.)

With the value determination procedures given by the authors, it can be shown for the mouse by clear estrous cycle curves that the ovarian hormone is also effective by oral administration. Approximately a twenty times greater amount is needed, however, *per os*, than is effective subcutaneously. Important conclusions may be drawn from this experience for therapy. The active value of the best ovarian preparation for oral administration tested, was never over one mouse unit per single dose. If a mouse unit

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is placed as a basis for the assigned requirement *per dosis*, the authors calculate that 500 dragees *per diem* would be required for a preparation. However, the question whether a mouse unit will be sufficient to attain an effective amount of hormone in the organism, is more than questionable on the basis of experiments on rats (five times heavier in comparison with mice). From determinations on the blood of women, it could be calculated that 50 to 150 mouse units circulate in the total amount of blood. If we estimate at 1 to 2 days the duration of the effect with the unusually stable ovarian hormone, that amount must be given in this period (through substitution therapy in deficiency of ovarian function) which takes into consideration the fact that only 1/20 of the hormone value comes to active development by oral administration.

The Content of the Human Pituitary in Melanophore Hormone. — K. Ehrhardt. (*Münch. med. Wochenschr.*, **76** : 321, 1929.)

The author examined 50 pituitaries of human corpses in order to test whether that agent which brings the frog melanophores to expansion (melanophore hormones) is regularly contained therein. The results of investigation are: (1) The melanophore hormone is almost regularly contained in the human pituitary (in 48 of 50 cases examined). (2) The melanophore hormone is also visible in the pituitary of old people and of the newborn. (3) The melanophore hormone was missing in the pituitary of a patient who died of paralysis and in a patient whose autopsy showed typical Laennec liver cirrhosis.

In conclusion, the author states: there exist in adolescence and even in childhood pituitary adenomas amenable to radiotherapy. When they are accompanied by osseous lesions which characterize gigantism or acromegaly, their diagnosis is easy. In the absence of osseous lesions and especially with symptoms of infantilism, the differential diagnosis between these adenomas and tumors of Rathke's pouch offers great difficulties. In doubtful cases when radiography of the skull does not reveal supra- or intra-sellar calcifications considered to be pathognomonic of tumors of Rathke's pouch, the possibility of adenoma must be thought of and radiotherapy be resorted to, at least as trial, to replace it by surgical treatment as soon as aggravation of symptoms principally of visual disorders, shows the ineffectiveness of this test.

Organotherapy in Cancer. — Rouss... Sergent. (*J. praticiens*, **43** : 319, 1929.)

According to the few observations report... by Naamé the idea should not awaken ... physicians that organotherapy in cancer c... play a rôle as active treatment. The obser... tions reported merely show that the gene... condition of the patient was improved. ... would be inadmissible to speak of a cu... Moreover, Sergent was never able to obser... improvement in the anti-cancer center ... Villejuif; he does not mention recover... observed such as those reported by Naamé.

Pituitary Adenoma of Adolescence and of Childhood Amenable to Radiotherapy. — A. Béclère. (*Rev. neurol.*, **1** : 463, No. 3, Mar., 1929.)

Gigantism and acromegaly either associated or isolated are the clinical manifestations of chromophil adenomas. Gigantism always begins before the age of 20 years, either at the beginning of adolescence or often from childhood, sometimes before the period of puberty and sometimes after it. Such was the case of a young girl of 16½ years in whom the author obtained the first lasting success with radiotherapy. This was 20 years ago and results have been permanent.

The form which is principally ophthalmic with or without symptoms of hypopituitarism, is the clinical manifestation of chromophobe adenoma. Dott and Bailey report in detail the observation of a chromophobe adenoma of adolescence with partial infantilism erroneously diagnosed as a cyst of Rathke's pouch, operated by transfrontal route with considerable improvement of the vision and irradiated later.

In some cases of gigantism the syndrome of infantilism is more marked and more complete simulates the clinical picture of tumor of Rathke's pouch. Finally among the observations of pituitary tumors more or less improved by radiotherapy, which Dr. Sc... mon reported to the International Neurological Congress in 1928, three concerned children from 11 to 12 years.

Precocious Glandular Obesity with Optic Atrophy. — F. Terrien, H. Schaeffer and J. Blum. (*Rev. neurol.*, **1** : 798, No. 5, May, 1929.)

The patient, a child of 5 years, weighing 32 kg., presented bilateral optic atrophy with

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white papillae and excessive obesity, involving the trunk and members, but predominating at the pelvis, buttocks, pubis and lower members, whereas the face, neck, feet and hands seem almost immune, as in the adiposogenital syndrome. This child presents a bilateral cryptorchidism; the sella turcica is abnormally enlarged; the thyroid seems small. There is no neurosomatic sign; intelligence is normal. Wassermann reaction is negative in the blood. The obesity and blindness seem to have developed parallel from the first months of life. In this case the author questions whether the optic atrophy is dependent upon the chiasmatic compression by a pituitary neoplasm or if the blindness and obesity do not arise from the same heredosyphilitic cause.

Studies on the Influence of Substitution in the Thyroxin Molecule on the Action of Thyroxin. — Abderhalden and Werthheimer. (*Zeitschr. exp. Med.*, 63 : 4-5, 1929.)

Closely related combinations of thyroxin were tested for their action with respect to the development and growth of tadpoles and axolotls as well as for gas metabolism in rats. On the whole fourteen combinations were tested. In the first place the problem is to determine definitely whether the specific action of the thyroxin bound to the iodid atom in the molecule, either wholly or in part by Cl or Br, could be substituted. The de-iodized thyroxin proves inactive in substitute combinations, a fact of particular significance, in general it proves active when in higher concentration. This holds good even for di-iodid thyroxin, that is after cleavage of one iodized oxy-phenyl group of the thyroxin. There is naturally, the possibility that the substitution product of thyroxin in the organism will be changed back; it is also possible that the action of thyroxin itself is not strongly specific.

Concerning the Biology of Placenta Extract. — Gräfenberg. (*Klin. Wochenschr.*, viii, 1376, 1929.)

Injections of placenta extract into animals gave a negative Allen-Doisy reaction. In human beings in which an injection is justified following hemorrhage in pregnancy, they have a diagnostic value. Placenta extract works favorably in the interruption of internal secretions.

Of Course the Patient Came Back

The young woman with dysmenorrhea who receives palliatives will return, because the disturbance of menstruation is still present. But sooner or later she "tries" another physician. Endocrine therapy which gradually relieves the pain by correcting the faulty menstrual process makes a favorable impression on the patient and her family.

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Atrophy of the Genitals and the Hormone of the Anterior Lobe of the Pituitary. — K. Erhardt. (*Münch. med. Wochenschr.*, **76**, No. 30, 1929.)

During a ten months observation of the blood and urine of a 35 year old patient with intense atrophy of the genitals and chronic paranoid mental disturbance, there was found a permanent positive reaction to the anterior lobe of the pituitary. In contrast to this very rare case, the next almost inexplicable observation is a relatively frequent transient positive reaction to the anterior lobe. This was found, though in no way regularly, in women castrated by means of the X-ray and in totally extirpated women, in cases of genital carcinoma, uterus myomatosus, epithelioma of the chorion, acromegaly and pituitary tumor, at the beginning of the menopause and in climacterium praecox, in amenorrhea, lipoid kidney and after the transfusion of 500 cc. of blood from a pregnant woman. On the basis of over 300 cases (experimental results of 2000 tests) the reliability of the Zondek-Aschheim pregnancy reaction has been confirmed.

Attack of Hypersomnia in a Patient with Thomsen's Disease: Remarkable Action of Insulin. — J. A. Barre. (*Presse méd.*, **37** : 1029, 1929.)

In an individual afflicted with Thomsen's disease there occurred at times, or daily, attacks of uncontrollable lethargy, deep and of long duration, out of which he could be aroused only with great effort.

Daily injections of 7-10 units of endo-pancreatic extract (insulin) caused this condition to disappear rapidly. Sleeplessness replaced the lethargy and the treatment had to be stopped.

Concerning the Endocrinology of and Therapy of Pathological Menstrual Hemorrhages in the Age of Development. — E. Glaesmer. (*Münch. med. Wochenschr.*, **76** : 406, 1929.)

It is a question of therapeutic experiment and result in a great series of menstrual anomalies in girls between 16 and 22 years who in the majority of cases exhibit "irritable hemorrhages" and in the preponderant number of cases a more or less marked genital hypoplasia.

A treatment of these irritable hemorrhages must *a priori* strive against an influencing of the follicular apparatus. The author attempted to exert this influence through cholin. Injections of cholin gave the same action in a mal experiment as radioactive irradiation. Cholin is a constant constituent of many sues. Owing to its blood-pressure lowering fect a hormonal property opposite to the adrenalin action is ascribed to it. The therapeutic experiences of the author are limited only the field of the increased hemorrhages accompanying hypogenitalism at the age of development, and are favorable throughout. The results of the treatment were almost entirely good. In just as startling a manner, however, cholin acted on puerile hemorrhages resting on infantile basis. The most suitable preparation for cholin treatment proved to be borate of cholin. Cholin is superior to weak irradiation, since it requires neither expensive apparatus nor difficult technique and renders possible much more accurate dosage.

The Internal Secretions and the Problem of Rejuvenation (Experimental and Clinical Trial). — N. E. Ischlondski. (*Progrès méd.*, **44** : 767, May 4, 1929.)

The scientific study of the problem of rejuvenation is founded on the following biological conception: the genital glands secrete a specific hormone into the blood which circulating in the organism assures the development, then the preservation of the specific sexual constitution, one of the most characteristic pictures of youth. The most intimate relations exist between the genital glands and all the rest of the endocrine apparatus; the decrease or increase of internal secretion of the genital gland reflects on the activity of the other endocrine glands such as the pituitary, thyroid, etc. The aim of rejuvenation is reduced to stimulating the activity of the whole complex of the endocrine glands by the inoculation of an internal secretion, most frequently the sexual secretion. Without this intermediary stage, without the endocrine apparatus as a whole, there can be no question of a general rejuvenation. There are three stages to be distinguished in the story of the practical realization of the problem of rejuvenation. In the beginning we were limited to the transplantation of genital gland from a young animal to an old. The success of the operation in small mammals is unquestionable. In man this operation can not be executed for two reasons. (1) A practical impediment — the absence of human materia-

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for the transplantation. (2). A scientific consideration: the fate of each transplant depends on the regenerative capacity of the animal organism. This latter power is definitely manifested by lower animals and diminishes progressively in the more differentiated organisms.

In the face of the impossibility of transplantation of the sexual gland in man, the investigators have sought other means of action on the apparatus with internal secretion. Steinach himself tried to replace homoplastic transplantation of the gland by ligature of the canal deferens of the gland of the aged organism. Voronoff decided to use heteroplastic material (glands of anthropoid apes).

The author considers the results obtained by heteroplastic transplantation to be due to non-specific protein therapy. He arrives at the conclusion that the surgical method of rejuvenation viewed from the practical viewpoint at least at the present time, loses its importance. In his personal works on the application of the internal secretion of the genital glands the author made efforts to elaborate a chemico-biological method having as goal the extraction of the pure sexual hormone to be injected into the blood by parenteral route. A series of systematic works in the indicated direction has shown that a great quantity of the stimulating substances is found in the region of the hepatic tissue, embryonic tissue and placenta. Towards the end of the year 1924, the author was able to extract the genital incretion in its active form. Before undertaking the study of the action of the isolated internal secretion he had to elaborate an objective criterion to determine its action scientifically. The product given contains the active genital secretion only in the case where the introduction of this product into the organism realizes all the modifications in secondary sexual characters which Steinach was able to obtain by surgery. If this condition is not accomplished, the product can not claim the name endocrine.

The results of investigations on the rejuvenation of old, enfeebled animals were very encouraging. The experiences of the author prove not only that an effect of regeneration of the animal organism may be produced but also that the result obtained represents an actual rejuvenation, since it signifies a very distinct prolongation of life.

The author then began to systematically study the effect of the extract on man. Cases of senility in subjects from 60 to 82 years of age (32 cases); cases of psychic old age (4 cases); cases of precocious senility at the age of 34 to 50 years (31 cases); definite cases of weakness or complete arrest of sexual function in men aged 32 to 55 years (22 cases); cases of sexual insufficiency and hypo-development related to general asthenia in young girls (12 cases); cases of decrease of general metabolism and asthenia with varying etiology (11 cases); severe forms of anemia in the two sexes (18 cases). After treatment with the extract the patients showed an increase in strength and physical resistance.

One of the early signs of the action of the secretion was the restitution of normal sleep. In all patients a considerable increase of appetite was soon noted. There was increase of weight. A beneficial effect on constipation was also noted. In all cases where objective disorders of the blood were observed, these disturbances disappeared. There was a considerable increase in the number of red blood corpuscles. The action produced on sexual function enfeebled by age or prematurely was very remarkable. Even in cases of prolonged and resistant impotence treated unsuccessfully by various methods the author succeeded in raising considerably or restoring *in toto* the lost function. It is very important as characteristic of this action that after a treatment of short duration (12 injections) the action continues to increase and develop during long months after the treatment to become stabilized definitively. Relative to the restitution of the weakened or absent sexual function in women, most frequently in asthenic and underdeveloped young girls, 1 to 3 injections of feminine internal secretion suffice to cause a reappearance of menstruation. The author also mentions the beneficial action of the secretion in cases of disorders of the menopause: in cases of amenorrhea and dysmenorrhea. Quite an exceptional rôle may also be given to the action of the secretion on the psyche. An important rôle belonging to the second category of influences of the secretion on neuropsychic activity of the organism is also described: the action on memory, attention and capacity for concentration, the influence on the skin also presents considerable interest from the scientific as well as the practical viewpoint; it becomes more elastic as turgescence increases. During the experiments on ani-

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mals a considerable increase in resistance of the organism to infections due to the action of the secretion was noted. This was also observed in man.

The secretion does not act directly on the separate functions but regenerates the mechanisms of the organism itself: in the first place the internal secretory apparatus and the central nervous system. From the theoretical viewpoint this signifies that the fundamental principle of the influence does not present a substitution of substances lacking in the blood but rather a specific therapy of stimulation of activity of the endocrine glands.

The Action of Parathyroid Hormone on Tetania Parathyreopriva. — A. W. Elmer and M. Scheps. (*Klin. Wochenschr.*, 8 : 1407, 1929.)

On the basis of extensive researches the authors came to the following conclusions. Parathyroid hormone has a specific action on Tetania parathyreopriva.

The action of the parathyroid hormone surpasses by far that of other mediums. Treatment with parathyroid hormone by subcutaneous injection acts, within 5 to 15 hours in such a way as to quickly ameliorate the clinical evidences of tetany. In the worst tetany cases, where immediate aid is necessary intravenous injection of parathyroid simultaneous with the subcutaneous injection is required, which will bring apoplectiform recovery within 20 minutes to 1½ hours. The intestinal treatment with parathyroid hormone is also indicated in most of the more severe cases of tetany, especially in those in which other measures have failed.

Parallel with effecting amelioration of the clinical picture the parathyroid hormone influences the blood chemistry in that above all it intensifies the blood picture; it decreases the phosphorus and potassium. The influence of the alkali reserve and of the coagulation time is not constant.

The dosage of parathyroid hormone must be calculated individually and under the control of calcium content of the blood.

The duration of treatment with parathyroid hormone is varied. In acute cases with only transitory insufficiency it should only be administered during the existence of the clinical symptom; in most of the severe chronic cases it should be administered, similar to treatment with insulin, continually or with short pauses, and at best with simultaneous administration, *per os*, of calcium.

Evidences of a hypercalcemic syndrome were not constant.

The Properties of General Regeneration Hormones. — Fränkel. (*Arch. klin. Chir.*, clv, No. 2, 1929.)

In a first piece of work the author showed that the healing process after fracture of the femur presents a varied aspect in cases of bilateral fracture and particularly different when the fractures are not simultaneous. In a second essay Fraenkel showed that this variation reverts to two different hormones, to the plastic hormone and to the hormone of regeneration; their concentration in the blood varies even considering the state of tissue in regeneration. In this new work the author attempts to determine the action of the hormone. In his opinion the plastic hormone acts first for the development of new tissue and then prepares the tissue, through sensitization, for the action of the hormone of differentiation. Lastly it might have a threefold function: it stops the development of new tissue, at the same time it activates the differentiation and the destruction of these tissues. Its action on young regeneration tissue is insignificant, as on old tissue.

Observations on the Changes of Permeability by Means of Thyroxin. — A. Fröhlich and E. Zak.

The researches of these authors portend that permeability in March (tested in frogs bred in winter) is significantly poorer than in autumn (tested in frogs bred in summer). Treatment with theophyllin improves the poor permeability of winter frogs and in contrast decreases the better permeability of summer frogs for potassium iodide.

Further researches showed, for the case of potassium iodide, that, to a certain extent, the nervous system co-operates in the influence of theophyllin on the tissue, while the action of this diuretic in the case of grape sugar is without the participation of the nervous system. Now follows the researches of Cori, namely that the hyperexcitability of the sympathetic nerve in summer, which is indeed capable of overshadowing the effect of the simultaneously stimulated vagus, is dependent upon the thyroid gland which is active during the summer. It seemed of interest, therefore, to inquire whether, by the

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administration of thyroxin to winter frogs that had previously been treated with theophyllin, a modification would be induced that would be similar to that in summer frogs treated with theophyllin alone.

For this purpose edible winter frogs were preparatorily treated in March, 1929, with thyroxin. The animals remained under this process for about three weeks, they were treated in practically the same manner as those of March, 1927 and 1928, with exactly the same experimental procedure; four injections of 0.3 cc. Henning's thyroxin solution were given subcutaneously. These animals were then daily, in the usual manner, perfused with theophyllin and potassium iodide (Ringer solution containing 0.1 per cent potassium iodide).

The result of this experiment was that winter frogs previously treated with thyroxin plus theophyllin responded, in degree of permeability to potassium iodide, approximately the same as summer frogs treated with theophyllin alone; therefore it was possible the year round, to simulate the influence of the summer months in this respect.

Rectal Liver Therapy. — A. Hittmair. (*Deut. med. Wochenschr.*, lv, 398, 1929.)

In two cases of pernicious anemia that refused the oral administration of liver, a test was made by giving liver broth as an enema. In one case the test failed, the other case became profusely diarrhetic. In additional instances 300 gm. of liver from liver preparations, in suitable quantity was given daily in the form of suppositories. In some diarrhea again ensued, in some the test was satisfactory, but not so satisfactory as when liver was administered by mouth. In time the administration of small enemas with the addition of liver preparations will be tested.

Concerning the Relation between the Endocrine Glands and Abortion. — E. Imparato. (*Monde méd.*, xxxix, 793, 1929.)

It is not yet understood what is concerned in the recovery from abortion. The author offers a series of opinions of various authors and on the basis of his own observations he comes to the following conclusion.

From the literature and from his own experiments it can be concluded that abortion is allied with the insufficient activity of glands and that in the pathogenesis of this disease the ovary plays a significant part. It is true that in the treatment of the above mentioned disease with organotherapeutic products there have been both good results and failures, but with the limited knowledge we possess of the physiology and pathology of the internal gland secretions, one must be very cautious when he directs his attention to abortion or refutes it.

The Increase of Erythrocytes following a Secretin Injection Is Principally Traced Back to the Spleen. — F. W. Krzywanek. (*Pflügers Arch. ges. Physiol.*, ccxxii, 435, 1929.)

The influence of secretin solution from the dried small intestine (duodenum) of dogs was tested on normal dogs. In each case, at various intervals after the injection, a considerable definite increase in percentage of blood cells occurred, that varied between 22.5 and 34.5%. This finding coincides with the results of other authors; the explanation that this increase was a new formation or a thickening of the blood was refused for the reason that the factor in this case was the function of the spleen; for in animals with the spleen removed such a rise after secretin injection was not at all evident, or at least in only a very few cases.

Concerning the Biology of Placenta Extracts. — Gräfenberg. (*Zentr. Gynäkol.*, liii, 1795, 1929.)

Placenta extract derived according to the method of Coca showed in experiments with mice, a negative Allen-Doisy and a negative Zondek-Aschheim reaction. It was evident that the testicles of male animals treated with this extract were smaller than the testicles of untreated control animals. The extract effected no abortive action and did not respond in anaphylactic tests on guinea pigs, furthermore, no complement-building substance was derived in rabbits. In spite of these negative results in experimental animals the extracts were valid diagnostically in human beings. The albuminous extracts are a fine reagent. Skin tests on pregnant women often give a specific wheal picture, but a conjunctival reaction is not evident. One injection of the extract following hemorrhage intercepts pregnancy; however, an abortive action fails. The results with placenta extracts are favorable for the interruption of

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internal secretions. In its biological properties placenta extract shows noteworthy relations to allergic extract.

Folliculin in Amenorrhea. — Laffont and Chiapponi. (*Bull. Soc. Obstet. et Gynecol. Paris*, No. 6, 426, 1929.)

In a case of dysmenorrhea and amenorrhea a total recovery was obtained by treatment with folliculin. The doses administered were 60 units in 3 days. In another instance in which larger doses were given, the results obtained were not in accord with the others. Both instances demonstrate again that the influence of folliculin on menstruation is not yet comprehensible. Certainly the folliculin possesses an undoubted activity, but the ways and means of administration requires the proof of researches. Clinical observations and the results of research on the estrus in the laboratory must supplement each other.

The Value of Contractility of the Spleen Induced by Adrenalin in the Practical Clinic. — Jean Lerebouillet. (*Paris méd.*, xix, 79, 1929.)

V. Simone (*Minerva med.*, May, 1929) studied the applicability for clinical medicine of contractility of the spleen induced by the administration of adrenalin. Adrenalin gives satisfactory results in the diagnosis of latent malaria particularly in those forms in which the histological changes of the spleen have not yet brought about the contractility. In the treatment of malaria and the suprarenal insufficiency induced by it, it is profitable to combine adrenalin with quinine.

The adrenalin experiments can be adapted with caution in the diagnosis of cryptogenic septicemia, but only if the ejection of the microorganisms of the disease, stagnating in the spleen, do not threaten to become worse. In fact adrenalin can provoke the relapse to typhus and Malta fever or endocarditis lenta. Furthermore, one must always keep in mind the possibility of rupture of the spleen itself or of cysts or abscesses of the spleen, and hemorrhages which result from a violent expulsion of blood through the extension or constriction of the collateral veins, and instances of thrombosis of the splenic veins are also to be feared, therefore, adrenalin can only be used after great deliberation.

In therapy adrenalin can be applied to many cases of splenomegaly in which one has to consider a spleen tonus following the dis- turbance of the circulation; thereby a sort of functional splenectomy can be attained in certain diseases in which the hemorrhagic infarct of the spleen plays an important part as is the case in many forms of hemolytic icterus. Lastly, by preliminary adrenalin injections by means of which the blood held in the spleen will be evacuated precautions will be had against the loss of a great quantity of blood in splenectomy.

Liver Therapy of Anemia in Nurslings and Young Children. — Jerachmiel Ligum. (*Monatsschr. Kinderheilk.*, xliii, 513, 1929.)

The author treated twelve cases of anemia of various sources in children with liver diet. In prematurely born children this therapy induced an increase of hemoglobin from 62 to 74% and an increase of erythrocytes from 2,930,000 to 4,400,000 resulted. It is possible to administer large doses of liver to older nurslings much more readily than to the prematurely born. In one instance, with prematurely born treated with raw liver juice treatment had to be abandoned because the stools resulted. Children in the first year accept liver readily, however, in children that have a distaste for it, liver therapy does not act favorably. In one case dyspepsia followed treatment and no result could be obtained. In most children from 1-6 years good results were obtained with liver therapy and an increase of hemoglobin as well as erythrocytes resulted.

The action of the liver must evidently be founded in part on the iron content of the liver; more likely the profusion of vitamines in liver gives the significant results in treatment. Liver contains all vitamines, especially Vitamine A, B and C, in large quantities. Herz in Hamburg agrees that good results were obtained in the treatment of anemia of children with the liver powder of Merck. Dosage was commenced at 1 gm. of liver powder and was increased to 25 gm. Perhaps the technique with the nutrient medium will be successful in affording good, easily digestible preparations.

Clinical Diagnosis and Treatment of Pituitary Disturbance of Growth. — Lucke. (*Klin. Wochenschr.*, viii, 1476, 1929.)

The condition of primordial dwarfism, in which the individual is born abnormally small, is contrasted with the condition of

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pituitary dwarfism which exists when, in early childhood, in a previously normal individual, the function of the anterior lobe of the pituitary is impaired. In the ensuing disturbance of the growth process the bones show the first evidence. The development of the genitals remains stationary and involution does not take place. The state of the genitals accords with the other somatic development. True anterior lobe insufficiency shows itself in the arrest of development of normal intelligence in children. In very severe impairment pituitary cachexia occurs, an indication that, in older individuals, is the only evidence of the late appearing pituitary disturbance. The pituitary dwarf presents regularly an abnormal length of members with nether length and width in excess over the aggregate length. This state appears secondarily in the tardy development of the genitals. Fundamentally, the specific-dynamic albumin reaction and the blood sugar concentration are lowered. Often an eosinophilia is found in the blood. Changes in the sella turcica are seldom evident. As long as the ossification of the epiphysis has not taken place a year's treatment with substance from the anterior lobe of the pituitary can effect results, so that growth is noticeably improved and in females as further evidence of the efficacy of the therapy in an individual approaching puberty, the menses regularly ensue.

The Influence of Treatment with Spleen Extract on Lupus Vulgaris. — Artur Mahlo. (*Med. Welt*, iii, 971, 1929.)

On the basis of reports of Fliegel and Blayle concerning the healing of tuberculosis of the bone by the administration of raw spleen, the author treated three patients who had suffered for 15 to 19 years with lupus vulgaris, with spleen extract. Of this preparation of spleen (1 tablespoon is equivalent to 100 gm. fresh spleen) the patients were daily given 1 tablespoonful. Extensive improvement was evident locally as well as in respect to the general condition.

Concerning the Pathogenesis of Serious Conditions of Suprarenal Insufficiency. — G. Marañón. (*Presse méd.*, xxxvii, 1021, 1929.)

Among the instantaneous consequences of severe cases of the disease, the author mentions acidosis as a weighty one, if not the only one. Swingle stresses the fact that hypoglycemia and acidosis are both responsible, and the latter mainly is involved through inorganic sulphate and phosphate. Viale and Bruno rank among the factors the definite increase of blood viscosity (caused not by the loss of water but of plasma) and the radical conversion in lipoid metabolism. Likewise in all the worst forms of morbus Addisoni acidosis must be reckoned with before anything else, and therefore the author undertook treatment. He gave a diet rich in carbohydrates, followed by small insulin doses (5 units) with the addition of glucose (25 gm. in solution) three to four times a day, and next, alkali medication and caffeine.

Infantile Diabetes Treated for 5 Years with Insulin. — Mouriquand, Sedaillian and Mestrallet. (*Presse méd.*, xxxvii, 963, 1929.)

The authors present the case of a child who had lived in the hospital for 5 years and who, during this time, had been continually treated with insulin, in daily doses of 60-100 units. The child led a normal life and did not have a very strict diet regime. The urine eliminated amounted to 2-3 liters during 24 hours with a sugar content of 124.98 gm. and a blood sugar content of 5 gm. per liter. Its alkali reserve is good.

Concerning Intracardiac Injections of Adrenalin in Anesthetic Syncopes. — Perrin. (*Presse méd.*, xxxvii, 949, 1929.)

The author attempted the above mentioned method three times and concluded that as preliminary treatment it can be very efficacious. Everything must be ready in the operating room in order to give an intracardial adrenalin injection at a moment's notice.

Discussion:

P. Bertrand reported three cases of resuscitation of the heart with intracardial injection and Cotte reports of noticeable indirect results, so that he had to desist and he deemed it necessary to substitute another cardiac tonic with longer delayed activity. Chalier is skeptical concerning the above mentioned process, while Villard reports very successful results.

Rectal Treatment of Pernicious Anemia with Liver. — Hans Pulver. (*Therap. Gegenw.*, lxx, 294, 1929.)

In four cases of pernicious anemia very good results were obtained by the adminis-

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tration of liver through the rectum (hepatic powder with a liver value of 1:5 and 1:100). The compatibility for liver enemas and suppositories is on the whole good. Only in singular cases, in old people do complaints arise. Also in one patient the enema met with failure as it caused diarrhea and pains. A really successful liver therapy requires a very large amount of liver before a normal blood value is approximated or attained. Only then can one seek to preserve the remission with small quantities.

Further Researches on the Cardiac Hormone. The Action of the "Substances Actives." — R. Riegler and F. Tiemann. (*Pflügers Arch. ges. Physiol.*, ccxxii, 450, 1929.)

The authors could not corroborate the findings of Demoors and his collaborators who had reported that the "substances actives" derived from the Kieth-Flack nodes are the agents of automatism and as such are transmissible to the deficient or non-automatic activity of the heart parts, such as the isolated left auricle. The principle agent of the activity which was called "substances actives" is a non-specific substance existing throughout the organism, apparently belonging to the histamine group.

Experiments with the Problem of Pituitary Diabetes. — K. Velhagen. (*Klin. Wochenschr.*, viii, 1577, 1929.)

From the experiments of this author it follows that even with amounts of posterior pituitary hormone which have no physiological value, experimental evidence cannot be obtained that the blood sugar is a simple function of the proportion of the posterior pituitary hormone and insulin in the organism, and that it is not possible to induce a true case of diabetes by means of large doses of highly active posterior pituitary.

Concerning the Action of Kidney Extract on the Function of Contracted Kidney. — K. Stejskal. (*Klin. Wochenschr.*, viii, 1517, 1929.)

In seven cases of primary and secondary contraction of the kidney, decrease in blood pressure could be obtained by the intracutaneous injection of kidney extract and also of lipoid extract of the kidney. This action fails in genuine high blood pressure.

Discussion: E. Freund who obtained the extract added some general remarks to the report which culminated in the noteworthy complaint that students of internal medicine for the last ten years have had no interest in pathological chemistry.

L. Moszkowicz recalled the researches of Henschel in Basel, who with the aid of autolysates of various organs was able to create a specific action on the related tissue.

F. Necker was in doubt about the specific action.

E. Urbach reported on the intoxicating action of skin extracts.

On the Biology of the Placenta. — Rodekurt. (*Zentr. Gynäkol.*, liii, 1801, 1929.)

In two cases of hyperemesis a satisfactory result was obtained with treatment with placenta extract, in one instance a very marked success. Daily, 1-2 cc. was given intramuscularly (1 cc. equals 25 units). In three normal cases the influence of placenta extract was tested for the calcium and potassium content of the blood serum. The calcium content was always increased, in two cases likewise the potassium content. Folliculin to the amount of 8 units injected intravenously also gave after 6 hours a total calcium and potassium increase in the blood serum. Intracutaneous injection of this placenta extract as well as of total ovarian hormone, testifortan, thyroid gland oil, insulin, etc., gave no standard results.

Concerning Spleen Diet in Tuberculosis Patients. — P. Rüttgers and A. Kamsler. (*Beitr. Klin. Tuberc.*, lxxii, 1, 1929.)

The patients were given daily to eat 100 to 150 gm. spleen mostly in the raw state; the method chosen for administration was, for the most part, in the form of beefsteaks: lightly roasted on the outside and inside rare. In patients who did not tolerate this method of treatment doses of pulverized spleen extract (analogous to prepared liver extract) were administered. This diet was tested on 12 patients. Subjective improvement was evident in the greater number of cases. The temperature decreased, coughing and expectoration diminished. A falling off of the bacilli in the sputum was fairly constant. The often observed rise in hemoglobin content of the erythrocytes is important except that high mountain air had earlier induced a change

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in this respect. There was a favorable influence in the physical condition of the most severe cases also. The murmurs were drier; radiologically, the primary exudative foci showed progressively less productive character; in contrast, the cavities appeared the least influenced.

Constitutional Weaknesses of the Cardiovascular System in Young Children. II. — L. Doxiades. (*Ergebn. inn. Med. u. Kinderheilk.*, **35** : 98, 1929.) **Constitutional Weaknesses of the Cardiovascular System and Internal Secretion of Young Children. IV.** — (*Ibid.*, 140.)

Schittenhelm and Eisler have observed in healthy persons, after intravenous or *per os* administration of thyroxin a rise of respiratory metabolism and an acceleration of albumin metabolism. The blood undergoes a decrease in content of Ca : K. The hydrogen ion concentration experiences no characteristic change. In one patient in whom edema had occurred in the climacterium, total rapid disappearance of the skin symptoms followed treatment with thyroxin. The size of the heart was definitely reduced and the electrocardiogram was normal.

Relatively little is known concerning the fate of the thyroxin introduced into the organism. The oxidative processes increased by the thyroxin, above all, serve the reconstruction process in muscular activity (convalescence) in growth and development. Thyroxin serves the vegetative system and its action evidently lies in the regulation of the fixed equilibrium within the system. There is a report of earlier date concerning the action of thyroxin on the vessels of the heart. Thyroxin evidently produces a change in the permeability of the capillary endothelium, acting either directly from the blood or tissues, or indirectly, following the rise of the oxidative processes. In myxedema there is, evidently in consequence of the lack of thyroxin in the blood and tissues, a decrease of permeability of capillary walls with consecutive dilation of the venous ends of the capillaries, the venous subpapillary plexus and hyaline changes in the cells of the corium.

The author reports the case of a 9 year old girl with congenital athyrosis, who had been under observation since the 8th year. With the institution of thyroid gland therapy (thyroidin, 0.1, three times daily) in addition to improvement of the other disease symptoms, there occurred a favorable influence on the cardiovascular weakness. After 3 months of continuous treatment with thyroidin, the child showed splendid general condition. The consequent year of treatment with thyroid gland was successful in remedying the whole myxedema symptom. Today we trend away from treating myxedema operatively — through the transplantation of the thyroid. The oral administration of an organ preparation now is the best choice of method. The thyroid activity is regarded as specific, dependent upon the peculiarity of the iodin-albumin linkage in the substance. Exact dosage of the preparation is hardly possible. For chronic hormone treatment the author recommends the *per os* method; because of the possibility of appearance of additional symptoms, the intravenous method should be avoided in polyclinical patients. In mongolism thyroid gland treatment does not accomplish the same as in congenital myxedema.

Hydrops Articulorum. — O. Fellner. (*Med. Klin.*, xxv, 746, 1929.)

The author treated many patients who suffered from post-climacteric pains in the joints with placenta extract and good results were always registered. Preparations containing albumin were never utilized. In placenta therapy of hydrops articulorum intermittens it is certainly not a question of unspecific therapeutic effect, but rather one of hormone influence.

Concerning the Various Actions of Histamin and Adrenalin on the Blood Vessels in the Rabbit's Ear. — E. Flatow. (*Arch. exp. Path. u. Pharmakol.*, cxli, 161, 1929.)

Small quantities of adrenalin do not produce the same effect on the blood vessels in the rabbit's ear as similar treatment with histamin does. In intravenous injection adrenalin acts in opposition to histamin in concentrations which will contract the blood vessels in the rabbit's ear.

Circulatory Problems. — Frey. (*Med. Welt*, iii, 611, 1929.)

A hormone of the circulation is found in the urine and blood. The isolated hormone was injected intramuscularly into patients afflicted with angiospasm, twice daily, in small doses. The author presents a female patient who was quickly relieved of the angio-

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spastic symptoms in the hands, objective cyanosis, subjective tingling, after the injection. The hormone failed to elicit results only in a case of long-standing circulatory defect. In hypertonics the hormone treatment also achieved noticeable improvement, and progressive muscular atrophy was likewise favorably influenced by the injection of this new circulatory hormone.

Therapeutic Application of the Hormone of the Circulation. — E. K. Frey. (*Münch. med. Wochenschr.*, lxxvi, 814, 1929.)

The report of a female patient who had been successfully treated with injections of the hormone of the circulation. Relaxation of the angiospastic condition of the legs could be observed. In four patients with intermittent lameness a dose of 1/20 mg. for several weeks, given twice daily was sufficient to capacitate the patient. The action on hypertonics was good and in two cases of angina pectoris the coronary arteries were capable of being influenced.

Embolism and Thrombosis. — Fründ. (*Med. Welt*, iii, 610, 1929.)

Doses of thyroidin seem to have induced a suppression of post-operative thrombosis and embolism. The administration of thyroidin appears to be of real import and to have an influence on the composition of the blood and thence influences the coagulum. Reference was made to the rarity of thrombosis and embolism following goiter and Basedow operations.

Concerning the Relationship of Pituitary Gland and Hypothalamus to the Retention of Water. — E. Frank. (*Med. Klin.*, xxv, 679, 1929.)

The clinician who studies the action of substance from the posterior lobe of the pituitary gland in healthy persons and in those patients afflicted with retention of urine must come to the conclusion that there is involved here an incretion. The diuretic effect of the extract is not its natural capacity, but rather it enters if the pituitary substance is administered to narcotized animals or is introduced directly into the blood vessels. With the slow penetration after subcutaneous injection, there is always found in human beings and also in experimental animals, an inhibition of water diuresis. The powerful action of small quantities of pituitary substance on the retention of water in normal individuals is very evident in Vollhardt's water experiments.

If one administers at regular intervals, about every 3-4 hours, to patients suffering from diabetes insipidus, a subcutaneous injection of 1 cc. of an active extract, the patient is kept healthy as long as treatment lasts. The 24 hour urine output is immediately reduced from 10 L. to 1½ L. and under. Gorke observed in one case, on 3 test days, as much as 12 hours of anuria. The specific gravity of the urine rose extraordinarily.

Because of the knowledge that the substance from the tuber cinereum is an incretion carrier as well as an incretion storehouse, and that a vicarious, hypertrophic portion of the incretion organ is inseparably allied with it, the demonstrative force of the argument presented in favor of the existence of an isolated center of water control and with it the experimental evidence that diabetes insipidus rests upon an affectation of the nervous element at the base of the mid-brain is destroyed; the true endocrine origin of the disease is well established.

Folliculin, Insulin and Diabetes. — F. Rathery and M. Rudolf. (*Bull. et mem. soc. med. hôp. Paris*, **44** : 741, 1928.)

The cessation of menorrhagic hemorrhages was observed following injection of folliculin in some cases. In two cases of severe diabetes in women a combined treatment with insulin and folliculin injections had as result a decrease of urinary sugar, disappearance of acetone and oxybutyric acid excretion. In one of the two patients the doubled folliculin dose had the opposite effect. In an 11 year old girl, who had not yet menstruated, glycemia was increased through the combined insulin-folliculin medication.

The Basal Metabolism. — P. Liebesny. (*Wien. med. Wochenschr.*, **78** : 1247, 1928.)

The clinical significance of the determination of basal metabolism is dependent upon the information obtained thereby concerning the function of the thyroid. B. R. Hill has shown that in 54 cases in which no typical symptoms of myxedema existed but only disturbances of circulation, the basal metabolism fell to about 13-47 per cent below normal. Thyroid therapy effected cure in 12 cases, improvement in 38 cases and left only 4 cases uninfluenced. Eppinger showed that in some

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cases of edema, which had remained refractory to every therapy, the administration of thyroid tablets proved to be the best diuretic. This by no means indifferent therapy will be resolved upon all the more readily in such cases when the determination of the basal metabolism gives strict indication for it. Eppinger also showed that individuals with normal kidneys present an accelerated chloride metabolism with the feeding of thyroid substance and finds moreover that patients with exophthalmic goiter show a rapid excretion of sodium chloride whereas myxedema patients retain sodium chloride. Through the determination of basal metabolism it can also be determined whether it is a question of an exogenous or endogenous obesity and when in addition the investigation of the specific dynamic albumin action is added, one can decide whether this obesity is dependent upon functional disturbances of the thyroid, pituitary or sex glands and thus hit upon the proper therapeutic measures.

Relations between the Digestive Tract and Blood Diseases. — Laqueur. (*Med. Welt*, 2 : 1538, 1928.)

In Holland good results were obtained in pernicious anemia by treatment with liver and liver extract prepared according to the instructions of the Committee for Pernicious Anemia (U. S. A.). Liver therapy is also to be tried in secondary anemias when other therapeutic measures remain without success. 1.0-1.5 gm. of the liver extract used corresponded to 100 gm. fresh liver. In most cases 3, 4 or 5 gm. of the liver extract suffice, but 12-15 gm. may also be given. The attempts at biological standardization of liver preparations have until now been without success.

The Internal Secretion of the Salivary Glands. — Goljanitzki. (*Ergebn. ges. Med.*, xiii, 125, 1929.)

In earlier experiments the author determined the following facts. Besides the production of secretion the salivary glands also have an endocrine function. The characteristic influence of the salivary gland incretion is on the condition of nutrition. In young animals the salivary glands have an important influence on the growth of the animal. Galebski tested the problem of endocrine function of the parotid gland and found that the fluid derived from the parotid according to the method of Krawkow, is physiologically active, as is evident from the reaction on the blood vessels of the isolated rabbit ear and from tests on isolated rabbit and cat heart. On the isolated heart of these animals the fluid effects an inhibitory action for the most part. In five of six cases intravenous injection called forth a decrease in blood sugar that paralleled the amount of injected fluid.

These facts are evidence, therefore, that the parotid presents, besides an excretory function, a substance which acts on the individual organ as well as on the entire organism.

Endocrinology and Opotherapy. — G. Hallion and R. Gayet. (*Monde méd.*, xxxix, 411, 1929.)

From a general consideration of the administration of organ preparations in the clinic, the author reports, after mention of numerous contributions to the literature, concerning the administration of the following organ preparations: Liver, insulin, pituitary, suprarenal, thyroid gland, parathyroid gland and mammary gland. In an ensuing resume the diseases were enumerated in which organ preparations were administered with important or insignificant results. These are asthma, Basedow, cancer, diabetes, diphtheria, hemoptysis, cardiac neurosis, edema, insomnia and tuberculosis. For all these diseases the preparations used, the experiments and the results obtained were presented.

Skin and Venereal Diseases. — Max Joseph. (*Jahresk. ärztl. Fortbild.*, xx, 14, Skin Diseases, page 20, 1929.)

Pulvermacher presented the question whether the skin is an organ of internal secretion. Theoretically it is possible that the skin produces one of the parasympathetic tonic hormones and acts as a synergist with the suprarenal cortex, with which in this particular sense it is comparable.

Concerning the Rôle of Adrenalin, of Insulin and Glycogen Sugar on the Mechanism of Attacks of Angina Pectoris. — J. G. Katz. (*Fortschr. Med.*, xlvii, 303, 1929.)

Hetenyi worked with two cases of diabetes and cardiac sclerosis in which at the conclusion of every injection of insulin attacks of angina pectoris occurred, which were regularly excluded, however, if the patient

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received sugar simultaneously with the insulin. Strauss does not believe that direct injurious action of insulin takes place in the heart.

Chasanoff believes that the glucose contains a nutritive substance for the heart muscle. A series of experiments and clinical observations has shown that adrenalin and insulin are to be regarded as antagonists. The adrenalin circulating in the blood mobilizes the glycogen so as to transform it into glucose. Herter showed that intravenous injection of adrenalin induces glycosuria. Zuelzer determined that adrenalin glycosuria is excluded when insulin is administered simultaneously with the adrenalin. The chemical nature of insulin is not yet explained. Insulin acts not only on glucose, but also it incites changes in the metabolism of nitrogenous combinations, of fats and of lipoids. According to Krawkow, adrenalin distends the coronary arteries in the greater number of instances. Schwarzmann observed infallible antispastic activity of adrenalin in spastic condition of the heart. Some authors describe insulin as a vagotropic substance, others find a decrease in vagotonus and an abatement of spasmophilia through the use of insulin. Deicke reported on a case of angiospastic hemiplagia with motor aphasia, in which following the injection of 40 insulin units, hypoglycemic reaction occurred. The attack was renewed after two injections of 25 units, 6 hours after the second injection.

Concerning the Action of Post-Pituitary Extract on the Musculature of the Uterus. — Hermann Knaus. (*Zentr. Gynäkol.*, liii, 1162, 1929.)

The administration of pituitary extract to induce labor pains does not always produce the desired therapeutic effect. It is for example impossible, with the aid of pituitary extract to induce an abortion or to bring about premature birth. Therefore, it is quite inexplicable on what basis pituitary extract acts, for, before the normal termination of pregnancy, it can induce no labor symptoms or only impotent short ones.

Up to the present the explanation has been made that there is a weak sensibilization of the uterus for the activity of pituitary extract at this time of pregnancy. The processes which are concerned during all periods of pregnancy, during birth and the puerperium in the uterus, and which are significant for the reaction of pituitary extract can well be studied in the rabbit. In a well developed virgin animal, the tonus of the musculature of the uterus was markedly increased by pituitary extract. Intra partum, there occurs after the use of pituitary extract one of the most ideal forms of rhythmically increased contractility for the progress of delivery. (Curves.) Because of this property to release uniformly flowing waves of contraction, post-pituitary extract is undoubtedly the best ecbolic. Twenty-four hours post partum the rabbit uterus is no longer capable of showing response to pituitary extract: the contractions analogous to those effected during the process of delivery. (Curve.) Forty days post partum a reaction similar to that in the infantile organ occurs after the use of pituitary extract. Depression of the muscular activity of the uterus is the base for the defective reaction to pituitary extract. Likewise the musculature of the uterus loses its power to react to extract of the post pituitary under the influence of corpus luteum.

Concerning the Influence of Administration of Thyroid Gland on Albumin and Fat Metabolism. — B. Kommerell. (*Biochem. Zeitschr.*, ccviii, 112, 1929.)

Two fasting experiments were undertaken on a dog in an interval of 5 weeks; during both fasting periods thyroid gland was fed. Representative of the action of feeding thyroid gland there occurred a basal metabolism rise of 30.5 per cent. This increased consumption of calories was defrayed on the average by 31.3 per cent albumin combustion and by 68.7 per cent fat combustion. The loss of body nitrogen during hunger, under thyroid gland activity reached almost double its original value.

The True Acidity in Isolated Portions of the Male Genital Apparatus of the Rat and Its Hormone Limitation. — Y. von Lanz. (*Pflügers Arch. ges. Physiol.*, ccxxii, 181, 1929.)

On the basis of his own observations the author determined that the true acidity in isolated portions of the male genital apparatus is not due to spermatogenesis, but rather to the existence of a generative gland substance in general. Bilateral castration differentiates the epithelium and determines the H-ion concentration of the secretion of this gland independently of the blood. The testicular

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hormone is active also after ligature of the ductuli efferentes. Apparently it was not absorbed in the epididymis.

Transplantation of Preserved Ovary. IV. Transplantation of Desiccated Ovary. — A. Lipschutz. (*Virchows Arch. path. Anat. u. Physiol.*, **272** : 245, 1929.)

Transplantation of totally desiccated ovary into the kidney of castrated male guinea pigs is always ineffective. By grafting ovary not completely desiccated, endocrine activity of the mammary gland apparatus occurs, which can become so intense that milk is formed. The endocrine action lies in a new formation of hormone in the grafted material in the organ of the host animal. Microscopic examination shows that the organ presents follicular development. The preceding damage to the organ does not inhibit the endocrine activity.

Investigations on the Origin of Creatin or Creatinin in the Animal Organism. — E. Abderhalden and S. Buadze. (*Zeitschr. ges. exp. Med.*, lxv, 1, 1929.)

As a result of the observations of various authors who, by the administration of thyroid gland substance induced evidences of creatin or creatinin, a test was made to determine whether the addition of thyroxin to muscle broth to which guanin had been added would influence the formation of creatin or creatinin. Hence it was evident that thyroid gland incretion caused the formation of creatinin and only without the addition of guanin.

Experimental Investigations on Corpus Luteum. — L. Brouha and H. Simonnet. (*Presse méd.*, xxxvii, 591, 1929.)

Corpus luteum extract, injected into normal female rats causes the suppression of the estrous cycle, provided the dosage is large enough. The genital tract assumes an appearance similar to that observed in castrated animals. With smaller doses a condition is established suggestive of a pseudo-abortion, without the characteristic estrus, but with the development of the uterus. With weak doses extention of the period of estrus only is obtained. In sexually immature animals the extract preserves the first estrus. In castrated animals no development occurs either in the uterus or in the sex glands. The extracts act on the estrous phenomena evidently in such a manner as to suppress the production of folliculin, but not its activity, for if folliculin and corpus luteum extracts are simultaneously injected the latter does not prevent the action of folliculin.

Hormone of the Anterior Lobe of Pituitary as Related to the Male Genital Tract. — L. Brouha and H. Simmonet. (*Presse méd.*, xxxvii, 591, 1929.)

Daily intramuscular implantation of portions of the anterior lobe of the pituitary show that this gland exercises a remarkable stimulating action on the male genital tract (rat, mouse). The activity of the anterior pituitary extract varies with the method of preparation and often with the dose administered. If the active principle which is contained in the urine of women at the beginning of pregnancy is used, there may be regularly observed a striking change in the genital tract of sexually immature animals, similar to that in adults. With extract of anterior pituitary prepared by alkaline method a definite development is obtained when small doses are employed and in contrast, an intensification or a retrogression with larger doses. We do not yet know whether this activity is referable to two antagonistic substances, or to a single substance which is active variously when injected.

The Zondek-Aschheim Pregnancy Reaction. — R. Brühl. (*Deut. med. Wochenschr.*, lv, 696, 1929.)

1. A positive result with the pregnancy reaction of Aschheim and Zondek gives very definite evidence of pregnancy. The negative result of the reaction excludes pregnancy with 100 per cent surety.

2. It is very evident that in the anterior lobe of the pituitary gland at least two hormones are formed. The one effects maturation of the follicles and is found usually in the urine of climacteric and castrated females, the other influences the formation of corpus luteum and is especially evident in pregnancy.

3. The hormone could not be demonstrated in the urine of mares in foal or cows with calf.

Organ Extracts in Their Action on Immuno-Biological Processes. — Pockels. (*Münch. med. Wochenschr.*, **76** : 770, 1929.)

Animals difficult to immunize were made good producers of antibodies by the injection

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of spleen extract. Spleen and lung extracts were administered orally to human beings in order to determine the active di-immunization. A specific influence was derived.

Insulin and Nutrition Depots. — A. Löw and A. Krčma. (*Biochem. Zeitschr.*, **206** : 360, 1929.)

The author studied the problem of how insulin, administered under various conditions affects the carbohydrate capacity of fat. The mouse served as the experimental animal.

The experiments show that a marked lessening of liver carbohydrate is induced after insulin injection. The beginning of the decrease can be determined 1½ hours after the injection. The decrease in liver glycogen is to be accounted as a direct action of insulin. In fatty tissue only inconsequential changes of carbohydrate content could be observed. The contrast with the action on liver tissue is important. It proves that insulin acts differently on fatty tissue as compared with the liver. The observations made at that time, namely that in fasting rats, more glycogen was found in the fatty tissue than in normal animals, permits the conclusion that carbohydrate can also be formed in the fatty tissue. The experiments of the author make it evident that the lobule organ can claim this function.

Concerning the Treatment of Milk Retention. — Walter Mestitz. (*Münch. med. Wochenschr.*, **76** : 782, 1921.)

The painful retention of milk, especially in sensitive women, must be actively combated. In this case diuretics are useful. Because thyroidin is a good diuretic, Kraul gave thyroid gland substance as treatment for milk retention and obtained good results.

Cell Formers and Cell Forms of the Blood. I. Changes in the Blood Formers during Complete Cure of a Granulocytosis. — W. Stockinger. (*Zeitschr. ges. exp. Med.*, **65** : 27, 1929.)

The author was able to determine that in granulocytosis, adrenalin acted to cause an increase of cells in the blood. The less this is, the worse off the general condition of defense in the organism. The cell increase after adrenalin is effected by the entrance of large unformed cell elements into the blood circulation.

Further Investigations on the Relationship between the Pituitary and the Ovum with Its Accessory Glands. — Hermann Siegmund. (*Münch. med. Wochenschr.*, **76** : 776, 1929.)

Following the implantation of rather large amounts of anterior pituitary tissue into infantile female mice, there appeared evidences of premature estrus due to the premature mobilization of hormone incretion in the ovary. After the implantation corresponding to high dosage it is even possible in the pregnant mouse to arouse the latent follicle of the ovary in pregnant state and cause proliferation and luteinization of the follicle cells. However, it is not possible to demonstrate estrus symptoms in the vagina during pregnancy neither could the ovary be forced experimentally to further incretion by the administration of anterior pituitary incretion. The release of the excretory function of the ovary, *i. e.*, the evacuation of ripe ova, could not be ascertained by the author. The researches performed according to various physiological methods all speak for the inhibition of each ovulation during the time of function of the corpora lutea. The author reports that the pregnancy test of Aschheim is exclusively reliable. Many contributions deny the control of the sexual function by the pituitary; the more prevalent perception that the ovum and its accessory glands have an active effect on the expiration of sexual function must be correct.

Hydrops Articulorum Intermittens. — H. Schlesinger. (*Med. Klin.*, **25** : 746, 1929.)

Many authors report that the therapeutic reaction in hydrops articulorum intermittens is unimportant. As may be seen from the literature, the disease is associated with the function of the female genitals. It occurs after prolonged puberty or after lactation in an abortion or parturition. The author applied therapeutics to this etiological association, and treated the patient described with placenta extract, throughout 5 months one injection every second day. The swelling was lessened, it did not last very long and it was no longer painful. The interval between attacks, which formerly was 8 days long, now was 12 days. The author believes that still better therapeutic effects may be obtained by the administration of stronger extracts — those given were quite weak.

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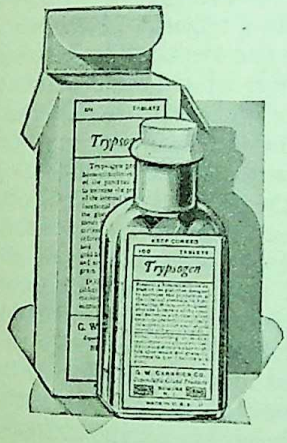
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Text Book Opinion

"The opposers of the oral method must remember that it will not produce the immediate and dramatic result that injection produces but then it does not expose the patient to the dangers of hypoglycaemic reactions nor the increasing dread of the needle."

(W. M. Crofton, *An Outline of Endocrinology*, 1929.)

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Test of Insulin-Induced Hyper-Hypoglycemia in Normal Subjects and in Pathological Syndromes (Emaciation, Obesity, Diabetes). — F. Moutier and L. Camus. (*Arch. mal. app. dig. et mal. nutrit.*, **19** : 297, 1929.)

The matter taken up in this article concerns a combination of a hyperglycemic and a hypoglycemic process an assumption depending on the hypoglycemic reaction of one person. However, one can not draw unconditional conclusions from work on emaciated individuals; indeed several of the thin persons observed by the author reacted strongly to the insulin test and presented quite variable results when insulin was given in therapeutic feeding. In any case it is determined that the test never did the thin people any harm. Hypoglycemic symptoms occurred only in persons with intense bulimia. Patients with dysthyreosis and some with sympathicotonic symptoms reacted quite easily. The test is also valuable for the comparison of the activity of insulin preparations of various origin.

Contributions to the Study of the Importance of Blood Glands for the Digestive Tract. The Action of Adrenalin and Insulin on the Secretion of the Succus Entericus. — B. A. Schazillo. (*Arch. Verdauungskrankh.*, **45** : 264, 1929.)

It has long been known by the clinician that the patient with hypothyrosis suffers from obstipation and the patient with hyperthyrosis suffers from diarrhea. Marbé, after feeding dogs with thyroid gland, observed a rise of intestinal secretion. The study of the action of adrenalin and insulin on the secretory function of the intestine has not only a theoretical interest, but also a great practical interest. The author undertook investigations on this problem, and found:

1. That the irritating action of subcutaneous injection of adrenalin — particularly at the height of digestion — is not favorable to digestion after meat extracts have been consumed. One gains the impression, therefore, that in this case the irritation is caused by an irritating substance produced by the intravenous injection of the incretion medium. Adrenalin in subcutaneous injection increases the activity of the sympathetic nerve element in the organs. At the culmination of digestion, however, the same quantity

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of adrenalin can increase the irritating effect on the animal only when given intravenously.

2. The irritating action of small doses of insulin on dogs is elucidated; on the basis of the investigation, it is to be assumed that the secretory process of the intestine was influenced both by adrenalin and by insulin. Insulin arouses the intestinal secretion in fasting dogs as well as at the culmination of digestion.

Influence of Internal Secretion on Dermographism. — G. P. Sanna. (*Med. Welt*, 3 : 530, 1929.)

The author has studied the variation in color, the time of appearance and the duration of dermographism in persons to whom had been given a high dosage of various internal secretion substances. Thyroid gland, suprarenal, pituitary, testicular and ovarian substance were administered *per os*. One hundred individuals were tested, of whom twenty served as controls.

Ovarian preparations (extract of the generative glands of lower vertebrates) brought out red, superficial dermographism with significant lessening of time of appearance and disappearance as well as the entire duration of the symptom itself. Besides the reaction was very intense: reflex dermographism.

Male generative glands (testicular extract of lower vertebrates) gave almost the same symptoms.

Thyroid gland preparations called forth a very pronounced, superficial, red dermographism, often accompanied with lateral white streaks, with definite lengthening of the time of onset and disappearance of the symptoms and great increase in the duration. The degree of severity was somewhat diminished.

The same symptoms were called forth by entire suprarenal extract, but the reaction was stronger, and more easily provoked.

With pituitary extract no definite action on dermographism was obtained.

The Functional Significance of Isolated Portions of Pituitary Gland. — A. Biedl. (*Endokrinologie*, iii, 241, 1929.)

On the basis of numerous observations it is now a well known fact that the anterior lobe of the pituitary contains a hormone capable of effecting the maturation of the sex glands. With consideration of the information that, in mice, the administration of large quantities of anterior pituitary hormone causes complete luteinization of the ovary overdosage in the form of a single large application of mouse units rather than long-continued parenteral application of anterior pituitary hormone is to be guarded against. Whether the anterior lobe incretion bears any relation to the carbohydrate metabolism, incidentally has not yet been determined for this instance.

The pars intermedia of the pituitary with the help of its incretion influences the requirement and consumption of substances, the general variations, the constancy of body heat, as well as the activity of isolated vegetative organs. The extensive information which we have gathered concerning the action of the extracts of the pars intermedia and posterior lobe gives evidence of the metabolic action of these parts of the pituitary. The question of where this active substance originates is not argued, nor is its hormonal nature generally acknowledged. Kamm and his colleague have shown that in pituitrin there is not a question of a single substance, but rather of several substances. The substances possessing either promoting or inhibiting activity on diuresis, according to existing conditions, seem to be contained in the fraction with pressor activity. The fat metabolism was influenced in such a way that after administration of pituitrin there occurred a considerable falling off of fat in the blood and a lessening of the ketone bodies.

The pituitary incretion acting on the center of vegetative metabolism can interfere indirectly in the function of the animal nervous system.

The pars nervosa and the adjoining stalk were found to have no incretory significance.

The functional significance of the pars tuberalis is not explained.

Endocrine Disturbances in Childhood. — Rudolf Neurath. (*Wien. klin. Wochenschr.*, 42 : 617, 1929.)

In the last stages of embryo life and soon after birth a definite overweight of the sex glands and cortex of the suprarenals occurs, that is evident in the anatomical size and in the quality of the skin and hair. Besides the intensified growth of the sex glands an increase in metabolism, due to unusual increase in hyperactivity of the thyroid gland, is characteristic for puberty; growth in height at this period is fostered by the anterior lobe of the pituitary. In adolescence the sex

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glands attain prominence; metabolism is undertaken by the hormone of the thyroid gland and the adrenal system and the lobule apparatus of the pancreas become more and more important for consumption and metabolism. Congenital thyroid gland defect is evident in the characteristic symptom of myxedema. In children this form is developed soon after birth.

There are also constitutionally hypothyroid individuals who have great need for hormone or whose thyroid gland functional capacity is greatly lowered — torpid adipose persons with lowered basal metabolism.

Also the temporary hyperthyroidism producing obstipation in newborn infants, which is always associated with the obstipation of the nursing mother, must be mentioned. The treatment of sluggishness of the bowels in both mother and child is promptly effected by thyroidin. In no phase of endocrine disease has substitution therapy acted so extraordinarily and showed its efficacy as in the treatment of hypothyroidism and athyrosis. Substitution therapy is accomplished by the ever increasing improvement of production of the hormone of the thyroid gland. As a daily dosage for nurslings thyroidin was given in tablet form of 0.1 gm., older children were given as much as 0.3 gm. The action of the hormone on the physical symptoms as well as on the psychic deficiencies is important. The endocrine function of the suprarenals is twofold. Recently, E. Schwarz performed investigations from the viewpoint of modern embryological opinions to shed light on the problem of interrenalism. In order to bring out all the evidences of interrenal syndrome depending on suprarenal hypertrophy, we have only to admit that the excessive activity of the suprarenals on the sex-determining gene complex of the chromosomes is such that the factor bound to the X-chromosome is impaired either by its own mitigation or by that of its opposing medium. Accordingly, the zygotic sex-determination is capable of being influenced by hormones.

Method of Increasing and Decreasing Secretion of Milk at Parturition. — Michel Wachtel. (*Zentr. Gynäkol.*, **53** : 987, 29.)

The attempt to cut off as quickly as possible an existing milk secretion, or not to "allow" the milk secretion to occur, is important in cases of intrauterine death of the fetus; further in women who have suffered a miscarriage in the later months of pregnancy, or whose offspring has died soon after birth. The congestion and tension of the breast full of milk is very painful to women. The treatment of this uncomfortable condition is most easily and simply effected by thyroidin. The earlier torment inflicted, of having the women go thirsty or to stem the function of the mammary glands by purgatives has become superfluous. After the administration of thyroidin, besides greater permeability of the tissues and influence on the osmotic oncotic pressure, there occurs a dispergence of the white blood corpuscles, for the increase of albumin and the decrease of globulin and fibrin. The result, therefore (Starlinger) is a much augmented capacity for swelling and a greater power to take up water. Kraul mentions the fact that he gave this thyroid gland preparation too, in painful condition of the breast during menses and obtained results. The author reports on twenty women to whom he gave early in the day and in the evening, 1 thyroidin tablet 0.3 and at midday he supplemented this treatment with 1 tablet of diuretin 0.5 gr. The treatment was continued for 3 days. Milk secretion did not occur at all. No harmful consequences have ever occurred.

Communications on the Activation of Adrenalin by Thyroxin. — T. Zimmermann. (*Biochem. Zeitschr.*, **206** : 369, 1929.)

The author undertook investigations to determine whether the activity of adrenalin could be influenced by the secretion of the thyroid gland. Following this the decrease of the glycogen content of the musculature after adrenalin injection was determined, and then the action of similar doses of adrenalin was noted after a thyroxin injection had been made. From all these tests it was learned how variable is the action of adrenalin. After adrenalin 1:10,000 there was a decrease of 21.8 per cent; with adrenalin 1:1000 this was found to be 25.28 per cent. The glycogen content of the liver with adrenalin 1:10,000 amounted to 1.79 per cent (resp. 2.16 per cent) with adrenalin 1:1000, 0.90 per cent.

If adrenalin injection is made 6 hours after a thyroxin injection, the diminution of glycogen in the muscle amounts to 37.6 per cent, the liver glycogen dropped to 0.257 per cent. Hence upon consideration of the

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thyroxin alone it follows that the thyroxin increases the activity of adrenalin for carbohydrate metabolism.

A Case of Cryptogenic Pernicious Anemia Which Proved Refractory to Simple As Well As Combined Liver Therapy.—Emile Weil. (*Paris Med.*, **19** : 416, 1929.)

Report on a case of cryptogenic pernicious anemia diagnosed as such clinically as well as by post-mortem examination. The patient, who had shown a remarkable improvement throughout a month of combined liver and insulin therapy, a few weeks later suffered a relapse and became entirely refractory in this stage to liver-insulin therapy. The author emphasizes the fact that too little observation has been made on those cases resistant to liver therapy, and he was supported in this opinion by Fiessinger and Tixier.

Severe Hemorrhage after Delivery. Non-Operative Treatment. Cure.—Voron and Pigeaud. (*Bull. Soc. obstet. et gynecol. Paris*, No. 3 : 225, 1929.)

In a 21 year old primipara, 2 days after spontaneous delivery, there occurred rise in temperature with chills and on the 10th day severe hemorrhage, which ultimately assumed a menacing aspect and made remedial measures necessary. The patient received only ergotin injections. Then, because the pulse became worse and further, anemic symptoms appeared, the patient was given injections of pituitary besides the ergotin injections, whereupon the hemorrhage was at once diminished, despite the noxa of a transport for eventual hysterectomy, and was entirely stopped within 23 hours by repeated pituitrin-ergotin injections.

Concerning the Relationship between Psoriasis and Ovarian Function. — E. Vogt. (*Monatsschr. Geburtsh. u. Gynäkol.*, **31** : 385, 1929.)

The hormonal theory always plays an important rôle in the explanation of psoriasis. Since the theory of purely thymogenic origin is so disputed, it might appear that the thymus gland plays a part in conjunction with the sex glands. The author reports on four cases in which the relation between the origin of the skin disease and the activity of the female sex glands seems quite certain. Case 1 gave evidences three times of this skin disease which first appeared in the 12th year, before the beginning of the menses (which began in the 14th year); the second time, after the birth of the first child, when amenorrhea of lactation was present; the third time, soon after the commencement of the menopause. In the second case psoriasis occurred in the course of amenorrhea of lactation; in the third case, after roentgen amenorrhea in a 50 year old female patient; in the fourth case after operation, radically, of a myoma. Basing observed that the disease appeared after the physiological amenorrhea of pregnancy; Scheuer observed a pronounced aggravation of the symptoms during pregnancy. Practically, hormone substitution therapy with ovarian preparations is to be recommended in the treatment of psoriasis, the most protracted and severest of those diseases requiring treatment; it may be recommended all the more since effective, active ovarian preparations can now be prescribed, to be taken not only parenterally but also orally. Further it may be noted that psoriasis has been treated repeatedly with insulin and good results ensued. From this one can assume a purely endocrine action of the pancreas hormone. However, there can also be the matter of a vitamin effect, the insulin working as a vitamin agent. Indeed the pancreas hormone contains abundant amounts of vitamin D.

Concerning the International Standardization of Drugs. — L. E. Knaffl. (*Wien. klin. Wochenschr.*, **41** : 1495, 1928.)

The Hygiene Organization of the League of Nations has suggested all the methods of standardization of drugs, also such as can be standardized by biological method. As regards pituitary extract, the Conference is of the opinion that the desiccated preparation of the posterior lobe of fresh pituitary prepared by acetone extraction, which has been proposed by Prof. Voegtlin at the Edinburgh Conference, is suitable to be accepted as international standard preparation. For the biological standardization of the oxytocic activity the test on the isolated uterus of the virginal guinea pig according to the Pharmacopoeia of the United States, 10th Edition, is recommended.

For the estimation of the action on the blood pressure comparative investigations on anesthetized dogs or on decapitated cats are recommended. For the determination of the antidiuretic action the test on the unanesthetized dog, on the healthy human being or

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in patients with diabetes insipidus is regarded as suitable. The Commission is of the opinion that in the event of the antidiuretic action being due to a third substance, there is the possibility of expressing the activity in antidiuretic units of the same standard powder. Still further investigations are, however, necessary to establish the unity and strength of the standard preparations of the different firms with respect to their antidiuretic action. In all cases a unit should be that which corresponds to the action of 0.5 mg. of the standard powder.

As international standard preparation for insulin, the desiccated preparation of hydrochlorated insulin is recommended, which was established by a resolution of the Edinburgh Conference of the Medical Research Council of Great Britain. One mg. of this standard corresponds to 8 such insulin units (1 unit — 0.125 mg.) as were previously defined by the Insulin Committee of Toronto University. The appointment of a sub-committee is recommended which will submit proposals with regard to the permissible organic desiccated residue per unit and with regard to the testing of the strength.

With respect to thyroid preparations the Genoese Conference was of the opinion that the biological estimation of thyroid substance was not in general necessary, but the iodin content in specific union with the active substance can be considered as measure for the therapeutic value. In order to recognize any increase of artificial iodin content, for example with iodides, the estimation by the so-called acetonitril method (Reid Hunt and Straub) is proposed. As comparative standard for the biological testing a desiccated preparation from healthy thyroid with an iodin content of 0.2 per cent is recommended.



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Leiner's Dermatitis. — Szentléleky-Szász. (*Monatsschr. Kinderheilk.*, **40** : 362, 1928.)

In nurslings with exudative diathesis and in those who suffer from Leiner's dermatitis subcutaneous injection of ½ to 1 cc. posterior pituitary extract caused the skin to become very pale within a few seconds and the skin process often disappeared after 24 hours; at the latest, however, within 4 to 5 days. The more severe the skin changes the more intensive the pallor. In one case of Leiner's dermatitis, under the action of posterior pituitary extract, the liver swelling decreased in striking manner.

Better results were obtained with decrease of the dose. The more severe the process, the smaller the dosage; on the average 1/3 cc. twice daily, in all 4 to 5 injections. The edema which lasted for a long time with 1 cc., did not come into question with small doses. In severe eczema also favorable results were obtained with post-pituitary extract. J. Pilcher (Cleveland) gives subcutaneously or intramuscularly in eczema 1‰ extract of suprarenal to 0.1 to 0.3 cc., and obtains cessation of the itching.

Concerning the Question of the Decrease or Abolition of Labor Pains. — Hoehne. (*Zentr. Gynäkol.*, **52** : 2773, 1928.)

The slight degree of narcosis intoxication with ether or ethyl-chloride injures — in otherwise excellent execution — the activity of the labor pains on the bearing down process. For this reason the simultaneous intravenous injection of a pituitary preparation is important in such cases, and the substitution of Kristel's extraction for the lacking abdominal muscular pressure.

Insulin, Synthalin and Glukhorment. A Comparative Investigation concerning Their Action on Glucose Fixation through Cells. — E. B. Salen and T. Nyren. (*Acta med. scand.*, **69** : 69, 1928.)

Experiments with synthalin and glukhorment carried out under corresponding experimental conditions show an effect of increasing fixation of glucose for both these substances identical qualitatively with that of insulin. Under the supposition that glukhorment contains a substance identical with synthalin or closely related to it chemically, the assumption is justified that the effect of increasing glucose fixation observed is wholly conditioned through a synthalin-like substance present in the glukhorment. The experimental results of the authors support the opinion that the glucose fixation-increasing action of insulin is a specific insulin effect which also has an essential significance for the function of insulin *in vivo* (for its sugar-regulating function). The latest attempts to define insulin chemically (Abel and his associates) have led to results which speak rather for than against the assumption that the specifically active constituent of insulin can be a substance closely related to synthalin. The demonstration of a qualitatively identical action *in vitro* of all three substances is calculated to support still further the whole conception.

A Chemical Reaction to Vitamins and Hormones. — E. Christensen. (*Münch. med. Wochenschr.*, **75** : 1883, 1928.)

The extensive harmony between vitamins and hormones pointed out by E. Vogt, suggested the question whether hormones give the same color reaction as is obtained when vitamin-containing extracts are diluted with phosphoric pentoxide. Accordingly, preparations of ovary and testis were tested and in both the same reactions with phosphoric pentoxide were determined. Moreover, a large number of commercial insulin preparations were examined and it was found that all without exception gave a positive phosphoric pentoxide reaction, to be sure in very different strengths, which seems especially noteworthy. There came to light, therefore, with respect to the reactivity to phosphoric pentoxide, various differences between the individual brands of insulin, such as were earlier described concerning the albumin content. To what extent these differences parallel the therapeutic usefulness of the individual preparations must first be explained by further investigations.

Hypergenitalism and Macrogenitosomia. — Serdukoff. (*Rev. franç. endocrinol.*, **6** : 378, Oct., 1928.)

By hypergenitalism is meant the precocious appearance of puberty with the organism remaining in a state of infantile development. Cases of hypergenitalism are much less frequent than the various forms of insufficient development and hypofunction of the genital organs. In definite clinical cases the symptomatology of hypergenitalism or macrogenitosomia in women presents a

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complex of primary or secondary symptoms translating the abnormal precocious development and premature manifestation of the functions of the genital glands. Almost always following precocious development of the genital organs, there occurs an exaggerated development of the whole body, muscles and skeleton. In relation to this exaggerated development, at the beginning, the attention is drawn by the tall stature and by a considerable weight.

Finally as the affection develops there is precocious ossification of the epiphyseal zones and the tendency to growth stops. The height, in general, in cases of hypergenitalism does not reach dimensions such as are observed in gigantism.

Hypergenitalism or macrogenitosomia is of endocrine origin. The height of girls suffering with macrogenitosomia exceeds by a third or a fifth that of their comrades; their weight may be double the normal. From the constitutional point of view one does not always find congenital factors of functional anomalies of the genital glands. Frequently girls suffering from this disease come from fertile families (nine, twelve and fifteen children) with twins and even triplets. The precocious appearance of menstruation is also found. At times familial hypergenitalism is observed.

The tendency to increase in size in the course of macrogenitosomia is also manifested for certain secondary sex characteristics: mammary glands, development of hair, development of external genital organs. In addition to the morphological modifications of the genital organs the precocious appearance of menstruation is observed.

The syndrome of genital hyperfunction in both sexes is manifested in childhood and assumes the character of pathological manifestation of hyperfunction of the genital glands: Hyperovarianism in women and hyperorchism in men. Among the characteristic symptoms in males there must be cited an abnormal increase in height, the precocious appearance of pubic and axillary hair, and the enlargement of the genital organs; the psychological changes and voice changes; sexual desire appears prematurely.

Etiology and pathology show that hypergenitalism or macrogenitosomia represents a disorder of endocrine equilibrium. The literature shows that cases of macrogenitosomia may have a primary character, that is, when there are morphological modifications in the genital glands themselves; the secondary forms of macrogenitosomia are related to affections of the pineal gland and suprarenal cortex.

In the cases of primary ovarian macrogenitosomia the presence of such ovarian tumors as adenocarcinoma, folliculoma and sarcoma is most frequently encountered. In the secondary forms, an important position is occupied by the affections due to pathological states of the pineal gland. Most frequently, such an etiology is related to the destruction of the pineal by tumors (teratomas, gummas, tuberculomas, hydrocephalus). In such cases of destruction of the pineal gland, the latter is unable to restrain the appearance of genital manifestations.

Moreover, as frequent cause of precocious puberty, tumors of the suprarenals must be considered: these tumors are most frequently hypernephromas, from the morphological viewpoint, which implies the increase in function of the cortical substance. The suprarenal cortex, according to its functional role, presents a synergistic action with the genital glands. That is why it is natural that increase in the intensity of the functions of the cortex substance of the suprarenals should produce a stimulating action on the development and growth of the genital organs and also contribute to the development of the secondary signs and growth of hair.

Hypergenitalism is not always a monoglandular endocrinopathy (affection of the ovary, of the pineal or of the suprarenal) and cases have been described in which simultaneous lesions of the ovaries and suprarenals have been observed. In these complex cases of hypergenitalism, symptoms of Addison's disease were present. In the cases where the macrogenitosomia bears the character of polyglandular etiology, obesity may be added to the precocious increase in height and to the development of the secondary sex characteristics.

In certain typical cases, in the presence of a monoglandular endocrinopathy, the diagnosis does not present special difficulties. In other numerous cases, in the presence of a polyglandular etiology, the diagnosis may be difficult. On the one hand, it is difficult to discover the participation of the affected glands and, on the other, it is not always easy to differentiate hypergenitalism from gigantism. The examination of the epiphyseal zones may establish the boundaries of the

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hypergenitalism and the gigantism; at times radiography decides the question one way or the other. In gigantism, the epiphyseal zones remain ununited for a long time; whereas in hypergenitalism, with precocious puberty, the arrest of growth in height takes place towards the age of 8 or 10 years.

In complicated cases, to discover the etiology and differential diagnosis, the reaction of Luttge and Mertz may be used.

Prognosis is intimately related to the etiology and the degree of specific involvement of the endocrine glands. Certain slight cases may be regarded as a manifestation of an almost physiological hyperovarianism following which precocious puberty supervenes and a regular menstrual function. The prognosis becomes more complicated in the cases where following the appearance of precocious menstruation in children, a prolonged loss of blood occurs whose real cause is malignant degeneration of the ovaries: their total ablation does not always suffice to prevent malignant recurrences in other organs.

Where hypergenitalism is intimately related to infectious, syphilitic, tuberculous processes, specific treatment may give a positive symptomatic effect as far as cessation of the menstruation is concerned and regulation of the endocrine equilibrium. At times the regression of all the signs of precocious puberty is observed. Such a result is at times possible in the rare cases where the hypergenitalism has developed following a neoplasm of the genital glands, which has been subjected to radical ablation of the affected glands.

Treatment, according to the case, is directly related to the importance and character of the lesion of one or the other gland dominating this endocrinopathy. In the greatest number of the cases where a malignant affection of the pineal or suprarenals is involved, it is impossible to obtain cure. In certain cases, satisfactory results may be obtained with applicatior of roentgen therapy to the ovarian region.

Organotherapy gives an inconstant symptomatic result, although adrenalin is sometimes capable of arresting the flow of blood in precocious menstruation. Serotherapy by the serum of castrates does not give appreciable result in the cases of considerable hemorrhages. In the symptomatic treatment of hemorrhage due to precocious menstruation, one can at times apply irradiation to the spleen by the x-rays.

Recently the specific action of thallium has been mentioned. Thallium preparations would be capable of inhibiting the production of ovarian hormones and the processes of ovulation. It is also legitimate to employ them in certain forms of hypergenitalism.

The Different Forms of Involution of the Corpus Luteum in Women.—M. Lucien. (*Rev. franç. d'endocrinol.*, 6 : 356, Oct., 1928.)

In the ovary of the human female the regression of the corpus luteum takes place according to two special forms, terminating in the simple fibrous evolutive corpus luteum and the degenerative fibrous corpus luteum or corpus albicans. The involutive fibrous corpus, which may be considered as the normal termination of the lutein involution, results from the banal hyperplasia of the connective elements of the corpus luteum evolving simultaneously with the fatty degeneration of the epithelial cells which atrophy and disappear. This fibrous corpus is but an ephemeral duration and does not take long to amalgamate with and disappear in the ovarian stroma.

The degenerative, fibrous corpus or corpus albicans appears following the brusque involution of the corpus luteum; it is preceded by the necrobiotic degeneration of the epithelial elements and is manifested suddenly by the precipitation of fibrils amid the collagenous protoplasmic ground constituted by the mortified cells. It is the result of a metamorphosing degeneration. The corpus albicans, which has become a foreign body in the stroma of the ovary, remains there permanently. The formation of the corpus albicans may be considered as a pathological phenomenon in relation to the disturbances of ovarian vascularization. Similar processes of involution of the corpus luteum are of a nature to disturb the normal rhythmic functioning of the ovary and to result in quite a series of pathological manifestations in the genital apparatus of women.

Pharmacologic Investigations concerning the Effects of Placenta Extract.—J. Kosakae. (*Japan J. Obst. and Gynaec.*, **11** : 27, 1928.)

The author carried out experiments with a placenta extract and a preparation prepared from human placenta through hydrolysis

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splitting by means of acid. Both extracts had a stimulating effect on the surviving uterus of the rabbit and occasioned rise in tonus and increase of the pendulum rhythm in the surviving intestine. Moreover, through the action of this extract, respiration is increased, the blood pressure in the pregnant animal is raised, otherwise lowered. The author believes that he may conclude from his experiments that placenta extract presents a stimulation to the parasympathetic nervous system.

Thymus Gland. — Nitschke. (*Münch. med. Wochenschr.*, **75** : 1782, 1928.)

The author believes that he has obtained an active thymus extract from the thymus, which calls forth the complete picture of tetany, in animals. In addition a second substance may be obtained which markedly lowers the calcium content of the blood.

Concerning the Substitution Theory in Addison's Disease. — Lange. (*Münch. med. Wochenschr.*, **75** : 1740, 1928.)

Following animal experiments with injection of adrenal cortex extract, the author tried clinically the effect on patients with Addison's disease. In the patients he did not use extracts but the material used for the preparation of the extract, administered orally. The first patient had the complete symptom complex of Addison's disease and so great an adynamia that he could only remain out of bed a short while. In 8 weeks of treatment, in which 5 grams of substitution preparation were given daily, an essential change slowly occurred in the patient's condition. There was a gain in weight of 5 kg.; the adynamia disappeared entirely; the patient took walks of several hours duration without interruption or fatigue. The accumulation of pigment in the skin and mucosae definitely decreased. In a second patient under treatment for the past 3 weeks, a gain in weight of 2 kg. and an indisputable lessening of adynamia were noted.

Hyperthyroidism and Diabetes. Considerations concerning Diagnosis and Treatment. — Carrasco Formiguera. (*Med. Ibera*, **22** : 419, Nov. 3, 1928.)

In the author's personal series, which comprises 1,450 diabetics, there are at least 33 in which the existence of hyperthyroidism was suspected; 23 in which this disturbance was clinically very probable and 20 cases of certain diagnosis. Of these 20 cases there are three in which the nature of the glycosuria may not be diabetic; there remain, therefore, 17 cases of coexistence of hyperthyroidism and diabetes.

The author limits himself to some considerations on diagnosis and treatment. In the presence of a case of hyperthyroidism, diabetes must be thought of and an investigation made for glycosuria and induced hyperglycemia, in order to rule out non-diabetic glycosurias. If the curve of hyperglycemia is of diabetic type, it is a case of true diabetes.

The author has the impression that it is of frequent occurrence to fail to diagnose hyperthyroidism in patients qualified as diabetic. He refers to those cases of hyperthyroidism which do not present exophthalmos, or do not present visible goiter, but nevertheless a slight enlargement in size of the thyroid. In these cases in which nothing attracts the attention of the clinician, it is necessary to be guided by the sensation of asthenia and by the loss of weight which can not be explained by the diabetes, since digestive disorders, irritability, exaggerated emotivity, a tremor and tachycardia are frequently attributed to the diabetic condition.

The ideal procedure would be for the physician to systematically determine the basal metabolism in diabetics; but as this is possible only in the great centers of clinical investigation, the physician must search for some of the above mentioned symptoms of hyperthyroidism and in case he finds them, make a determination of the basal metabolism, the sole method of establishing the diagnosis with certainty.

One of the findings which has most frequently suggested hyperthyroidism to the author has been the persistence of loss of weight and strength or the failure to gain even after treatment of the diabetes has brought about a disappearance of the glycosuria with a sufficient diet to obtain a good state of nutrition.

In order that the basal metabolism test may have its full value, it is necessary that this test be carried on when the patient is not glycosuric and has been submitted to a diet that is not loaded with proteins and sufficient to cover the nutritive needs (which can be foreseen independently of the hyperthyroidism). Insulin has made it possible to completely eliminate the unfavorable influence

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of diabetes on hyperthyroidism; so that the prognosis will depend solely on the degree of thyroid disturbance.

Treatment consists in (1) eliminating or reducing to a minimum the factors which in addition to hyperthyroidism may be the cause of the raised metabolism. For which reason it is necessary to avoid the action of cold, to limit as much as possible muscular exercise and reduce the protein diet to the lowest limit compatible with the balanced nitrogen intake; (2) administering sufficient food to cover the energy requirements of the organism, abnormally raised by the hyperthyroidism; (3) increasing as much as possible the metabolic capacity of the organism, for which the necessary quantity of insulin is administered for the necessary amounts of glucose to be tolerated.

In the great majority of cases the adoption of these methods has as effect the rapid and more or less considerable improvement of the general condition, increase in weight, in strength, or at least maintenance of weight, decrease of tachycardia, and nervousness. At times this improvement of the general condition becomes very important.

As the plan of treatment described does not influence the hyperthyroidism at all, the result is that any increase in muscular activity or any decrease in the supernormal amount of food causes loss of weight and of strength and change for the worse in the general condition. In no case did insulin cause any improvement in the thyroid disturbance. For this reason, thyroidectomy, irradiation or anti-thyroid organotherapy will be necessary, according to the case. The author believes that in the majority of cases the better transition for the latter treatments is to be obtained by the administration of small doses of iodin.

Liver Extract and Tropical Anemia. — A. Díaz Albertini and J. Rodríguez Pérez. (*Vida Nueva*, **22** : 191, Sept. 15, 1928.)

The authors report the results they have obtained in many cases of tropical anemia by treatment with liver extract, four cases being reported in detail. The study of these cases again shows the remarkable action of liver in these anemias. Under the influence of liver the number of red blood cells increased considerably and at the same time the proportion of hemoglobin increased. In consequence, the general state of the patients improved notably, the diarrhea disappeared from the very beginning of the treatment and the tongue soon resumed its normal aspect. The authors kept control of the blood sugar of the patients, because experience has shown that by maintaining it at figures around 90 mg. per 100 cc. of blood, the most favorable results are obtained, and because in this way the appetite is stimulated and the protein diet may be amplified by the addition of carbohydrates (but not by fats which are poorly tolerated). In general, five units daily of insulin sufficed.

The authors call attention to the low monocyte count in advanced cases. These increase in number as the improvement becomes more marked and remain in relatively high figures among the normal.

On the other hand, the lymphocytes in general decrease in number, coinciding with the improvement noted in the processes, and in consequence, they have great importance from the viewpoint of prognosis.

The authors have not yet had sufficient experience with the therapy to speak of the future of these individuals. They can not tell whether the patients will have to continue taking liver extract indefinitely or whether the results obtained will be maintained causing the reactivation or a permanent improvement in the functions of the liver and perhaps an anatomic regeneration equivalent to a cure. At the present time, the authors believe that permanent improvement may be obtained in young individuals. This is not the case in older patients whose completely exhausted liver must be substituted for, and logically the liver treatment will have to be continued indefinitely in these cases.

In concluding, the authors state that a liver preparation with these properties constitutes a considerable advance in modern therapy. Next to insulin, it is the most beneficial force which has been realized in the field of medicine.

With liver extracts the authors have been able to obtain brilliant results in cases where a short time ago there would have been no successful therapeutic agent.

Movement of Water in the Organism. — Mautner. (*Deut. med. Wochenschr.*, **54**: 1824, 1928.)

The movement of water in the organism is dependent upon physico-chemical reactions, muscle contractions, etc. In the gastro-intestinal canal in which not only absorption

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but still more secretion of water takes place, it is the contractions of the intestinal villi which essentially influence the processes of water movement. Yeast extracts, for example, stimulate here. On the other hand, secretion and peristalsis influence the absorption. Nervous stimuli and hormones, for example, the absorption-favoring insulin by way of the hypoglycemic attack and pituitrin, further or restrain absorption. Concerning the complicated processes in the passage of water over into the blood, little is known. The mechanical pressure in the capillaries is decisive for the mechanism of the extravasation of water into the tissues. The essential regulation site lies in the liver, in which the contraction of the liver veins inhibits or enhances. In contraction of the liver veins there may result extravasation of water from the capillaries to the veins, so that following a drink of water a dripping on to the liver surface can be observed. Here also not purely mechanical but also hormonal influences are at work. In the kidneys too not only filtration or expressing but also vital processes and nervous influences are active. In perspiration an inactive phase likewise must be assumed through which the water can enter through skin or lungs. The water deposits are also involved in the regulation of the water stability, the activity of which is restrained through a regulating center. A diuresis inhibition proceeds from the cerebrum; the diuresis center lies in the vicinity of the tuber cinereum, of which one part is connected with the pituitary. Pituitrin, which streams directly into the third ventricle, acts as a stimulus for the part of the diuresis center situated here. The adequate stimulus for this center is probably the oncotic pressure of the circulating albumin and the changes of the blood albumin picture. In addition, nervous influences, salt content and reaction of the blood and above all glands with internal secretion play a rôle.

Clinical Value of the Ovarian Preparation Prepared According to the Method of Stern-Batelli. — A. Kogan and L. Libin. (*Arch. Gynäkol.*, **135** : 262, 1928.)

The frequent lack of result in the use of ovarian preparations encountered commercially may be explained by the fact that the ovaries like other endocrine glands, possess no store of specific hormones, but secrete them in the quantity in which they arise in the blood. An active preparation could therefore only be prepared when the gland concerned continues to live following its removal from the organism and can secrete its secretion products into the environs. The method of Stern-Batelli rests on this principle: the ovaries were cut into fine pieces, placed in Ringer's solution previously warmed to 38° and saturated with oxygen; 10 cc. of Ringer's solution to every 1 gm. of tissue. The tissue remains 20 to 30 minutes suspended under a supply of oxygen at body temperature; the fluid is frequently changed. Finally, the whole fluid is filtered and used without further treatment. For the most part, 50 to 100 cc. were administered once or twice daily per rectum. The preparation was given in 62 cases. In 12 women of 22 to 43 years, in whom the uterus and ovaries had been removed, and severe deficiency symptoms existed, increase of deficiency symptoms appeared during the first weeks of treatment, followed, however, by essential improvement. These women had previously been treated with organ preparations altogether without result. The same thing occurred with 8 patients in the climacteric with symptoms of ovarian insufficiency, in whom improvement was obtained through the preparation. Moreover, 22 women with amenorrhea (in part with underdevelopment of the genitals) were treated with this preparation. These women had also been treated previously without result with organotherapy. With the Stern-Batelli preparation regular menstruation was obtained in one part of these amenorrheic cases. Finally 16 patients from the Neurological Clinic (12 basedowoid and 2 with pronounced exophthalmic goiter) were successfully treated with this preparation. In order to effect complete stimulation of the ovaries a 4 to 6 weeks treatment is necessary.

Modern Treatment of Diabetes in Children.—R. Wagner. (*Wien. med. Wochenschr.*, **78** : 1139, 1928.)

If the diagnosis of diabetes has been made in a child, then insulin should be given at the outset even if sugar can be removed without insulin. For in the first place it is easier with this therapy to get rid of an infection to which the children are frequently exposed and secondly, with simultaneous treatment with insulin, more carbohydrate may be given to the child, which is of great

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importance in childhood. If a child is received in coma, 50 to 60 units are given intravenously as initial dose and the injections are repeated in small doses every 2 to 3 hours within the first 12 hours. When vomiting has ceased and respiration has improved, the doses of insulin must be lessened in order not to induce hyperinsulinism. Small children are very sensitive to insulin and easily become hypoglycemic. In this case, when an oral administration of sugar is not possible, 10 per cent glucose solution is given subcutaneously.

Acrocyanosis of Young Women. The Physiopathologic and Pathogenic Importance of Venous Hypertension and Ovarian Insufficiency. — M. Villaret and F. Saint Girons. (*Arch. Méd. Enf.*, **32** : 79, Feb., 1929.)

The authors have observed the existence of a syndrome characterized by three factors in a rather large number of patients ranging from 15 to 20 years: acrocyanosis, ovarian insufficiency and increase of venous tension. The young women have had irregular menstrual periods from the beginning of menstruation; obesity is at times important and is generally distinct. All present a very marked cyanosis of the hands, less marked of the feet, with edema and chilling; the disturbances are very marked during the winter where they terminate in painful frostbites; these frequently ulcerate and resist the classic treatment as long as the weather remains cold. Otherwise, the patients give no clinical sign of disorder or anomaly of the circulatory, respiratory, urinary or nervous system. However, in contrast to a maximum normal arterial pressure, their venous pressure is constantly increased.

It seemed to the authors that this syndrome was intimately related to the existence of ovarian disorders as shown by the irregularity of menstruation and the frequent obesity. It is a question of endocrine cyanosis, for ovarian organotherapy has given definite results, especially in one case (improvement of the subjective disturbances with improvement in the menstrual periods, indisputable decrease of cyanosis and slight fall of venous pressure).

The authors do not wish to give the impression that all cases of acrocyanosis are of ovarian origin but merely wish to show that some cases of this disturbance have this etiology. It appears also that the ovarian disorders which are the cause of the cyanosis and venous hypertension are solely disturbances of hypofunction. In fact one woman whom the authors had occasion to observe was suffering from obesity of thyro-ovarian origin with vertigo, headaches, sweating, increase of menstrual flow, and presented severe metrorrhagia whenever ovarian therapy was attempted. In this case of hyperovarianism the venous tension was not only not increased, but was distinctly below the maximum arterial tension.

The interest of the syndrome resides especially in its pathogenesis. Venous hypertension need not be dependent upon a cardiovascular affection alone but may also result from an endocrine alteration. It is also worthy of notice that the venous hypertension and acrocyanosis may decrease in parallel manner under the action of ovarian therapy.

Spleen and Rickets. — R. Soula and Cauquil. (*Paris méd.*, **18** : XIII, 1928.)

Rickets can only be an endocrine insufficiency of elaboration of sterins. This elaboration which under normal conditions probably takes place through the spleen and reticuloendothelial system, is insufficient in rickets. It can be corrected through irradiation and organotherapy.

Pituitary Dwarfism. — Dr. and Mme. Schiff. (*Paris méd.*, **19** : xxx, Jan. 5, 1929.)

The authors present a patient of 14½ years whose physical growth has been completely arrested since the age of nine years. At that time a syndrome of cranial hypertension expressed itself in intense headaches and vomiting. Two years later, the child became suddenly and totally blind. The headaches have persisted since that time. At the present time there exists a complete atrophy of the optic nerves, a slight hydrocephalus, a considerable enlargement of the sella turcica upon radiography. Outside of the dwarfism a fall of basal metabolism of 26 per cent and a testicular sclerosis were noted. The Borde-Wassermann test of the blood was negative in the subject and his mother. Specific treatment prolonged for 4 years, remained ineffective.

The authors discuss the indication for a surgical intervention (transphenoidal ablation, transfrontal puncture), despite the irremediable loss of the vision, and the

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utility of the radiotherapy, which would have to be very prudent because of the great radiosensibility of the nervous cells of the child.

Painful Vasomotor Disorders in a Case of Dysendocrinism. — M. Scharrenberger. (*Presse méd.*, **37** : 146, Jan. 30, 1929.)

The patient, a young man of 20 years, presented painful pricking of the hands and feet; at times, paroxysmal pain accompanied by pallor and coldness of the fingers and toes; at times cramps. Beginning at the age of 10, the present condition has existed since the age of 14 years. The disturbances came on without apparent cause. The subject was never able to do any appreciable work.

On examination there was noted a feminine habitus, a dysthyroidism and signs of sympathetic disequilibrium. The patient's hands were smooth, pale in color, warm to the touch, of weak muscular strength in proportion to the slenderness of his extremities, without pyramidal deficiency. Normal objective sensibility; no pain on pressure. In short, an association of endocrine sympathetic signs in a young man presenting painful vasomotor symptoms.

Concerning Hyperglycemia in Acute Disease of the Pancreas. — F. Bernhard. (*Deut. Zeitschr. Chir.*, **212** : 217, 1928.)

Hyperglycemia is an important symptom of acute disease of the pancreas. The cause of hyperglycemia is to be attributed to lack of insulin. For this reason, energetic insulin therapy is recommended in acute necrosis of the pancreas.

Investigations concerning the Influence of the Thymus on Muscular Activity. — O. Held. (*Zeitschr. Biol.*, **88** : 76, 1928.)

The author performed experiments with thymus extracts which were injected part subcutaneously, part intravenously and tested the influence of thymus preparations on the phenomenon designated as "apparent fatigue." This apparent fatigue is removed, as this experiment shows, by subcutaneous and intramuscular injection of thymus preparations. It is not the effect of an albumin substance. The action of thymus preparations is shown on the working muscle itself, whose ability for work is heightened. Control experiments with Ringer's solution were negative. Intravenous injection of adrenalin solution did not have the same effect as thymus preparations.

Studies of Calcium Metabolism in Certain Diseases of the Skin. — N. Burges. (*Brit. J. Dermat. and Syph.*, **40** : 279, 1928.)

Certain dermatoses are dependent on increased irritability of the nerve cells, caused by lack of calcium in the tissues. The results of treatment show that administration of calcium and thyroid preparations in dermatoses of nervous origin is of special value. Cases of urticaria, prurigo, eczema and those cases of cyanosis of the extremities and chilblains with low calcium content of the serum were considerably improved with calcium and thyroid therapy.

Hormonal Influencing of Sex in Animal Experiment. — Beyer. (*Med. Welt*, **2** : 1528, 1928.)

Resuming the experiments of E. Vogt, Beyer remarks that to the two possibilities of influencing sex — through undernutrition and overnutrition — the hormonal influence may be added as a new possibility. Through this the general law is supplemented, according to which in times of need, under abnormal living conditions more female young are born than male. In this way the preservation of the species is most certainly guaranteed. From this viewpoint the hyperfeminization of the new generation seems to be a sequel to the injuries undergone during the war.

Influence of the Glands with Internal Secretion in the Metabolism of the Bones. — Biedl. (*Med. Welt*, **2** : 1544, 1928.)

In embryonal life and shortly after, the interrenal system (adrenal cortex) and the sex glands are especially influential, on the contrary, the thyroid minimal. In the phase of puberty, the time especially of growth in length, thyroid activity appears in the foreground, and raises the metabolism. Here we also have hyperthyroid disturbances, the goiter of puberty. The proper growth glands are the thyroid and the pituitary anterior lobe. However, without the growth symphyses remaining open, growth is not possible and the symphyses remain open only so long as the development of the sex glands is not yet complete. Administration of thyroid

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substance can occasion changes in growth and proportions even in adults. The hyperthyrosis causes an excessive growth in length in the growing individual. Pituitary dwarfism can be improved by administration of pituitary substance. The pituitary anterior lobe is a growth gland. Premature development of the sex glands can also be influenced by feeding of pituitary.

Neuroses Conditioned by the Endocrine Glands. — F. Boenheim. (*Arch. Verdauungskrankh.*, **42** : 383, 1928.)

The author contributes histories of patients and disease pictures in order to draw the attention of physicians to the etiological significance of endocrine disturbances for neuroses, psychoses and hysterias. The recognition succeeds only through exact somatic investigation with respect to the endocrine function. The thyroid probably produces a whole series of different hormones so that in dysfunction of the thyroid the most diversified disease pictures can arise. Boenheim sees a corroboration of his conception of the endocrine genesis of many neuroses in the therapeutic activity of specific organotherapy, for example, whole pituitary suppositories.

A Case of "Ovarian Diabetes," Resistant to Insulin, Very Much Improved by Folliculin. — Carnot, Terris and Caroli. (*Bull. et mém. soc. hôp. Paris*, **44** : 738, 1928.)

A 36 year old patient, in whom diabetic symptoms and amenorrhea arose simultaneously. Daily excretion of sugar up to 100 gm., at times acetone, marked emaciation, distinct variations with the menstrual cycle. Neither dietetic nor insulin therapy had any effect. Following injections of folliculin, decrease of urine and blood sugar. Gain in weight.

Rise in Blood Pressure and Extirpation of the Spleen. — Hercher. (*Zentr. Chir.*, **55** : 2350, 1928.)

The author refers to the repeatedly observed threatening fall of blood pressure, which appeared following the use of spleen extract. The question whether it is a matter here of a hormone action or an anaphylactic manifestation is not yet clear. Can the rise in blood pressure following extirpation of the spleen be considered as an effect of removal of the organ, perhaps conditioned by a loss of an internal secretory principle of the spleen?

Internal Medicine and Chemistry. — H. Horsters. (*Med. Klin.*, **24** : 1441, 1928.)

A new branch of chemical therapy has arisen with the discovery of adrenalin: hormone therapy which can also be designated as constitutional therapy. Here medical chemistry in clinic and laboratory has celebrated triumphs with the discovery of insulin. In synthetic thyroxin a further important step in this field has been made. Liver therapy in pernicious anemia promises new discoveries in the ranks of substitution therapy. The important task is here reserved for the chemist to isolate the sum of the active principles and present it pure. The closest joint work with the clinic is indispensable for the experiment. In respect to the purification of organ extracts, however, nature orders a halt, according to all appearances, in that it has been shown that in a part of these substances a too extensive purification in the sense of the isolation of a chemically defined substance often leads to decrease of activity. In this connection the work on insulin must be remembered.

Diuretics. — A. Herz. (*Wien. klin. Wochenschr.*, **41** : 1378, 1928.)

Thyroid preparations act extrarenally in dropsy with lowered thyroid activity and in nephroses. Their use is contraindicated in cardiac edema, in nephrosclerosis, hematuria and hyperthyroidism. Control of the pulse and of the properties of the urine is absolutely necessary in thyroid medication. Thyroid tablets should be given in a dosage of 0.3 gm. at the beginning increasing to 2 gm. after about 2 weeks.

Practical Therapeutics

(*Continued from page 145*)

anism of action as the continuous absorption of minute amounts of nitrite ions, thus causing gradual relaxation and rest. He summarizes as follows:

"1. Variations in the chlorid content of the blood do not affect the arterial tension to any major degree.

"2. Administration of bismuth subnitrate causes a slight reduction in the chlorid content of the blood, as do other nitrates, through the production of a chlorid diuresis.

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"3. Administration of bismuth subnitrate assists materially in obtaining a reduction in arterial tension in hypertension, both in non-pregnant and pregnant cases.

"4. The therapeutic results are much better when arteriosclerosis is not marked.

"5. A method of evaluating therapeutic results in hypertension in terms of percentage return to normal is presented.

"6. The pharmacodynamic mechanism of bismuth subnitrate in hypertension is a dual one:

"*a.* Gradual vasodilation by continuous absorption of small quantities of nitrite (NO_2^-) ions.

"*b.* Reduction of the blood chlorid content by diuresis initiated by the nitrate (NO_3^-) ions.

"7. The fundamental value of bismuth subnitrate in hypertension lies in its property of breaking the vicious circle of vascular fatigue, hyperirritability, with more spasticity and fatigue and thereby permitting of physiologic *rest.*"

Hypertension is of unknown etiology as far as the ultimate causes go. The treatment, therefore, is partly symptomatic and expectant. Perhaps no condition claiming the attention of a physician requires so much individual study. The careful physician, however, can accomplish much in most of his cases.

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A Case of Intersexuality of Hermaphroditic Type. — G. Marañón. (*Med. Ibera*, 22 : 381, Oct. 27, 1928.)

The states of intersexuality in the clinic may be divided into the following groups: hermaphroditism, masculine or feminine pseudo-hermaphroditism, virilism and feminism, cryptorchidism and hypospadias, gynecomastia, homosexuality and other functional intersexualities, intersexualities of puberty and the climacteric, partial intersexuality in normal subjects. Of all these types of intersexuality, the most unusual is hermaphroditism. Nevertheless, it is probable that the true hermaphroditism, that is, the simultaneous presence of two sex glands in the same individual with the corresponding coexistence of the characters of both sexes, is much more frequent than supposed. In fact, in order to be certain of the existence of the mixed sex glands or ovary-testis, it is necessary not to limit oneself, as is generally done, to the examination of a single genital gland extracted during a surgical intervention, but the two glands must be studied carefully, since in the majority of cases the ovary-testis is limited to a single side and perhaps to one of the poles of the sex glands. For this reason, various cases diagnosed as pseudo-hermaphroditism, that is, of inverted appearance with normal sex glands, must be in reality true hermaphroditism incompletely studied. To this group belonged without doubt an intersexual who was exhibited at fairs in Spain and who was recently studied in the author's clinic. He is sixty years old and reports that he has menstruated up to about fifty years. His appearance is mixed. The distribution of fat, the comparative proportions of his pelvis, and scapular girdle, the pubic hair and above all the breasts are those of a woman. The hair and voice are masculine. He states that his instincts are also virile and that he has had frequent sexual relations with women. The genital organs show a penis the size of that of a boy of about 15 years, without urethra. This opens one centimeter below, and 2 cm. lower a small vaginal conduit opens. The labia majora have the appearance of empty scrotal sacks.

This case would usually be diagnosed as one of feminine pseudo-hermaphroditism; Pozzi labeled it such 26 years ago. The equal presence of both sexes, however, suggests a case of true hermaphroditism. In this case, however, as in others, an exact diagnosis could only be made after histological examination of the sex glands.

General Therapy of Skin Diseases. — Otto Kren. (*Wien. klin. Wochenschr.*, **41** : 1404, 1928.)

Organotherapy attempts to improve the function of diseased organs, or to replace

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their chemical function. As is well known, the endocrine glands also secrete substances peculiar to them, of which each one has a very special task to fill for itself in the body. These substances are the hormones. To carry out a correct hormone therapy, signifies being acquainted with the action and symptoms of abolition of function of the endocrine glands with their effects on the skin and the organism in general and treating them accordingly. In this respect it is to be mentioned that frequently not only one gland is disturbed in its function but the whole harmonious interrelationship of all glands, that, therefore, obviously several glands are functioning abnormally and for this reason call forth a disturbance.

Pulvermacher recently reported investigations, therapeutic results and experiments and arrived at results full of contradiction. One is, however, certain: Each of the endocrine glands can produce substances in disturbed function which sensitize the integument and so give occasion for the origin of a dermatosis. Whether the secretion itself forms a hormone, as is claimed by some authors, which is also involved in the course of the dermatosis, must be determined by further investigation. The type of treatment consists for the most part in the administration of the missing hormones or in roentgen stimulation of the organs concerned. In the administration of the hormone the subcutaneous or intravenous form of administration is in each case superior to the oral.

Animal Experimental Investigations concerning the Pituitary Anterior Lobe Hormone with Special Reference to the Reproductive Phases. — Schultze-Rhonhof. *Deut. med. Wochenschr.*, **54** : 1702, 1928.)

Typical changes are found in the vaginal mucosa even in castrated animals 72 hours following injection of ovarian preparations. Pituitary anterior lobe implant in still immature mice results in sexual precocity in 80 to 100 hours and simultaneously to change of the vaginal mucosa. In castrated animals, pituitary anterior lobe has no influence. In an infantile mouse even the implantation of the pituitary of an 80 year old individual had a marked influence. Infantile hypophyses implanted into infantile animals likewise result in signs of pronounced ovarian function, even when the implant came from animal fetuses; human fetal organs acted only to 50 per cent. Through simultaneous implantation of anterior pituitary and thymus, the origin of estrus was for the most part prevented.

Relations between the Digestive Tract and Blood Diseases. — Schottmüller. (*Med. Welt*, **2** : 1538, 1928.)

Liver powder gives the best results. In "liver remissions" increase in reticulocytes occurs after 1 week; after 8-14 days increases in erythrocytes and hemoglobin occur. The manner of action of liver is still unknown — hormonal or detoxicating? Analogous to liver therapy in pernicious anemia, spleen treatment is to be tried in hyperglobulia.

Arthur Hartmann

(*Continued from page 147*)

and relating to physicians. He attended meetings of many medical societies at which he sometimes contributed and sometimes presided; he abstracted material for these meetings as well as for several publications in which he took an interest. The journey to England and France was a kind of self-imposed apprenticeship through which he was able to bring to his own country the best knowledge and experiences of the workers in other countries. He served on Medical Boards in both active and advisory capacities. The desire to reform and improve medical study prompted Hartmann to make a survey of courses of instruction for physicians especially in England and France and also in other countries of Europe. He presented his findings in several essays and drew up a new system for Germany. As a member of the *Schuldeputation* in Berlin and as an official in charge of City Hygiene, Hartmann instituted a course of special training for school doctors, for it was his belief that physicians must be especially trained to handle children. He assisted in establishing a school for the instruction of deaf and dumb individuals based on the principles derived from his researches in this special field.

As evidence of a practical bent, there are several instruments invented by Hartmann, for use in the treatment of diseases of the ear, nose and throat. They are still in use under his name.

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The Theory of Insulin Action. — Schur. (*Klin. Wochenschr.*, 7 : 1983, 1928.)

Schur is of the opinion that insulin attacks the assimilation process in such a way that it effects the deposition of carbohydrate in the fat tissue and its transformation into fat tissue. Proceeding from this standpoint, the author undertook determinations of the total carbohydrate in the fat tissue with a new method, according to Dische and Popper, and constantly found quite considerable amounts of carbohydrate as well as a quantitative influencing of it through administration of carbohydrate. Insulin probably also has a direct effect on the deposition of lipoids. It appears, therefore, quite generally to have a furthering influence on the deposition of food substance ingested.

Porges, Vienna, proceeding from the viewpoint that even in normal individuals a diet rich in carbohydrate raises the carbohydrate tolerance, gave diabetics a diet rich in carbohydrate (with the use of large doses of insulin), thereby a diet rich in albumin but poor in fat with a considerable increase in tolerance as a result.

Discussion: Adlersberg is of the opinion, according to his experiments, that the retrogression of the urinary sugar in this form of diet is dependent upon an increased density of the kidneys. Minkowski, Wiesbaden, doubts this and considers the rise in tolerance obtained to be dependent upon the large amount of insulin used. Porges stresses that the rise in tolerance is also obtained without insulin and even with the use of insulin appears only when abundant carbohydrate and little fat are given, not, however, when little carbohydrate and a large amount of fat are given.

Nature and Treatment of Hyperemesis Gravidarum. — Runge. (*Zentr. Gynäkol.*, 52 : 2547, 1928.)

Insulin is no longer to be dispensed with in the treatment of hyperemesis. It is, of course, understood that care must be taken that carbohydrate be administered before the injections, either in the form of sugar water or, when that is not tolerated, in the form of rectal injections. To overcome the severe conditions of emaciation in this disease, insulin forced feeding offers quite an essential support in doses of about 5 units. The appetite increases, there is gain in weight. There is no question but that insulin is an extraordinary adjuvant to therapy in this condition. Runge is altogether of the opinion of Heynemann with respect to the specific action of insulin. It is as little a question of a specific effect in the insulin effect here as in any other remedy used up to the present in hyperemesis.

Action of Thyroxin on the Heart. — M. Nothmann and G. W. Parade. (*Klin. Wochenschr.*, 8 : 699, 1929.)

The sharply defined relationship between hyperthyroidism and cardiac symptoms, as well as the great rôle claimed by thyroid gland therapy due to artificial incorporation of thyroid gland incretion by the method of Kendall and Harrington, gave the authors the impetus to investigate the action on the heart of doses of thyroxin administered intravenously and perorally. They used for the experiments synthetic thyroxin derived according to Schering and employed the method of Schoeller. In the metabolism experiments conducted by Lublin, it was seen that this preparation acted to increase the basal metabolism.

The effect of thyroxin was observed on the healthy heart and on a series of cardiac patients. Report will be made later concerning their tests on thyroid gland patients.

In twenty patients, neither after intravenous (two doses, 5 mg. per dose) nor in *per os* administration (three times daily, 1 mg., 2-4 weeks duration) did they see any signs of hyperthyroidism whatever. The general condition was in no way disturbed.

The pulse frequency in persons with healthy heart showed, similar to the investigations of Baur and Loewe, no increase, if we accept as a psychic factor the rare occurrence of 10 beats increase per minute immediately after injection. Likewise irregularities of pulse were never induced. In three cases of absolute arrhythmia, a striking increase in frequency was observed after injection of small doses, which was less conspicuous after large doses. With intravenous injection of large doses the author was under the impression, often, that the pulse was noticeably slower.

The most important of the authors' investigations are concerned with the effect of thyroxin on the course of the electrocardiographic curve. In their normal cases neither was there any effect to stimulate the heart itself nor any other part of the body. The configuration of the auricle or ventricle complex was never altered. In cases of auricular

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flutter or auricular fibrillation with absolute arrhythmia of the ventricle the authors observed no increase in the fibrillation symptoms of the cord. After small intravenous doses of thyroxin, the often improved, increased discharge of the ventricle, running parallel with a striking increase in pulse frequency, was seen which can be spoken of as a cursory improvement of transfusion. In one case of entire dissociation based on luetic cardiac affection, neither was the sinus frequency increased nor were the secondary centers of the ventricle affected.

In conclusion, the authors state that thyroxin, of the forms of medication chosen by them, does not act on the pulse frequency or the course of the electrocardiographic curves.

Castration in Pregnancy. — Waldstein. (*Wien. klin. Wochenschr.*, **42** : 380, 1929.)

Both ovaries were removed from a woman with bilateral dermoid cysts in the second month of pregnancy, a normal termination of birth resulted in a child weighing 3500 gm. taken by forceps. The case was subjected to quite elaborate hormone study. The ovarian hormone content of the blood serum was quite like that of normal women. In desiccated extract of the placenta about 300 mouse units of ovarian hormone were determined, a rather insignificant amount, but as the investigations on the subject show, it can be indicated as normal, since even in normal placentas a similar amount can be found. From the above experiments the following conclusions were obtained:

1. Ovarian hormone does not originate in the ovary, but rather in the placenta.
2. The placenta does not store the hormone.
3. The hormone produced from the placenta was given into the blood *in statu nascendi*, for as much ovarian hormone could be found in the blood of the placenta as occurs in the whole placenta. By means of these investigations the theory of Halban appeared to be confirmed, whereby the placenta produces "active substances." This is none other than hormone.

The hormone of the anterior lobe of the pituitary was likewise evident after castration, as well as in other pregnant women, so that one can assume that production of the hormone of the anterior lobe of the pituitary was not affected by castration. From the urine of castrated women much less ovarian hormone was isolated than from that of normal pregnant women. The author believes in treating the castration symptoms after the termination of lactation with the hormone derived from the woman herself.

Four weeks after the castration operation the woman suffered a psychosis, for which she was promptly hurried off to a psychiatric clinic.

Sex Hormone in the Urine of Pregnant Women. — Leiv Kreyberg. (*Norsk Magasin for Laegevidenskapen*, **90** : 379, 1929.)

Ovarian hormone as well as pituitary hormone can appear in the urine. Ovarian hormone is found in the urine in a whole series of body conditions: in pregnancy, at the beginning of the climacterium as well as in certain forms of amenorrhea. In contrast to this, the pituitary hormone appears spasmodically, as it were, in the urine of initial pregnancy and can therefore serve as an efficient indication of early pregnancy. The author adds observations from which the changes in infantile sex organs of the mouse due to pituitary hormone from the urine of pregnant women are indisputable.

Concerning Specific-Dynamic Activity and Pituitary (Rat Experiments). — R. Nothhaas. (*Pflügers Arch. ges. Physiol.*, **221** : 763, 1929.)

By feeding substance from the cortex of the anterior lobe of the pituitary, a specific-dynamic activity occurred in rats in 14 days to 3 weeks (normal about 20 per cent) to a maximum of about 26 per cent increase. Therewith the basal metabolism fell.

Therefore the rat is a suitable test object with regard to the component of the anterior lobe of the pituitary, which initiates metabolism.

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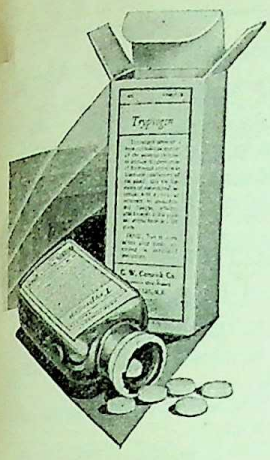
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Vol. XIV JULY-AUGUST, 1930 No. 4

The Journal of Organotherapy

A Record of Progress in the Study of the Internal Secretions and Metabolism

G. W CARNRICK CO., *Publishers*



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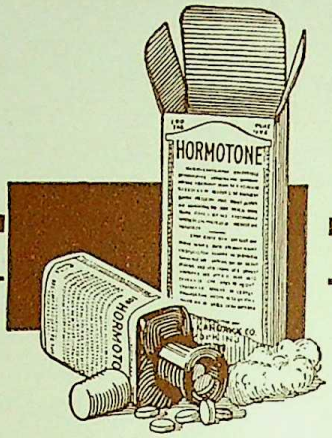
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What Trypsogen Does

TRYPSOGEN
Aids in the Utilization of Sugar.
Aids in Storage of Glycogen in the Liver.
Depresses a Relative Adrenal Hyperfunction.
Improves the Associated Defects of Digestion and Absorption.

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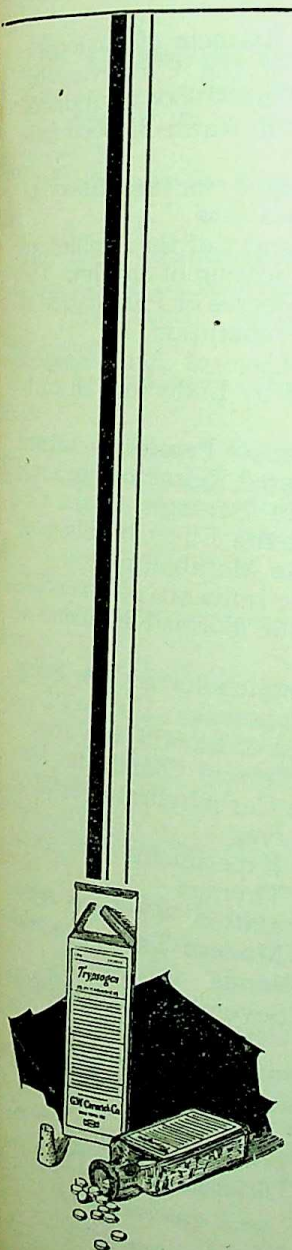
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What Authorities Say

¶ Pancreas preparations administered through the intestine "can be absorbed and can function to cause the utilization of sugar". (J. R. Murlin, *Endocrinology*, May, 1924, p. 339.)

¶ "The presence of something derived from the pancreas, either its digestive ferments or some internal secretion besides insulin, is necessary for the maintenance of normal metabolism." (Charkoff, Macleod and Markowitz, *Journal of Biological Chemistry*, 63, p. LXXI, February, 1925.)

¶ In reporting ten carefully controlled experiments with various pancreas preparations orally administered, Prof. P. J. Cammidge says of Trypsogen--- "Would seem to contain an antiglycogenolytic fraction which is absorbed from the alimentary tract". (*British Medical Journal*, Dec. 26, 1925.)

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(W. P. Graves, M. D., Professor of Gynecology, Harvard Medical School.)

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Rejuvenation and Stimulation of Sexual Activity

REJUVENATION and restoration of sexual function are not synonymous. Nothing can prevent the structural changes of age. Special functions, however, may be increased by endocrine therapy.

THERE is a very sharp difference between rejuvenation and mere stimulation of sexual activity. Rejuvenation implies a complete restoration to a condition of youth, not only the feelings and functional capacity but the entire actual and potential possibilities of the organism. Frequently, however, the word rejuvenation connotes something entirely different — the restoration of the sexual capacity. This use of the word has become particularly prevalent in connection with gland transplantation operations, rejuvenature of the vas, etc.

So far as therapeutic efforts at rejuvenation are concerned, they are hopeless from the beginning. No method or drug has ever been found which will stay the slow gradual tissue changes characteristic of the age process. These changes are inevitable. Professor A. S. Warthin states that they can not be regarded as disease, rather the whole process is a physiological entity and the result of involution processes inherent in the organism. The "major involution" is the aging process of the organism as a whole. Aging of individual organs is a "minor involution." The changes which affect the tissues of the body as a result of the age process are not simple, but, in general, active functioning tissue of all types is replaced by connective

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tissue. This slow process of involution proceeds throughout life and in later periods the structural alterations utterly preclude re-establishment of function at the levels of early life.

Rejuvenation must be considered from a dual standpoint — the exciting or therapeutic agent causing the rejuvenation and the reacting organism to be rejuvenated. Hygienic measures in general are rejuvenation measures, but the connotation of the term rejuvenation to both laity and profession refers to sexual rejuvenation so that the current concept has entirely lost the full significance of the term.

In the case of therapeutic attempts at "rejuvenation" with the sex glands, it may be remembered that they exert not only a sex specific influence on the reproductive system, but a general influence in increasing metabolism and tonicity of the somatic tissues as well. As a result of gland transplantation experiments and ingestion of sex gland preparations it has been possible to show beyond all doubt that the functional activity of the sexual system may be heightened and the general vigor of the body increased. Voronoff and others have given striking evidence of this kind. Steinach, by an entirely different method, succeeded in increasing the interstitial hormone production and achieved the remarkable results now well known to the world.

Very recently highly concentrated preparations of the active male sex hormone have been prepared by Gallagher and Koch (1) and by Funk, Harrow and Lejwa (2). In 1928 McGee, Juhn and Domm (3) published the results of their researches on the activity of extracts of bull testes, using the secondary sex characters of capons as a means of measuring the activity. Making use of the methods developed by Allen and Doisy, Frank and Gustavson and others, for extracting the estrous hormone from follicular liquid, placenta, etc., they showed that lipoids exhibiting the property of stimulating the growth of the comb, wattles and ear lobes of the capon can be extracted from bull testicles. Briefly summarized, they showed:

"1. A benzene soluble lipin fraction obtained from bulls' testicles when injected into brown leghorn capons causes growth of the comb, wattles and ear lobes.

"2. The amount of lipin material injected daily represents from 150 to 500 grams fresh testicle tissue.

"3. Although the reactivity of individual capons varies, these variations are of such a nature that this biological reaction can be used as a rough quantitative method for assaying such lipin preparations.

"4. Very frequently serious local reactions appear at the site of injection and much unabsorbed material may remain.

"5. When injected into bilaterally castrated hens good comb growth was induced.

"6. The crude lipin found in the benzene soluble fraction can be freed somewhat from non-potent material by fractional precipitation by methyl alcohol, ethyl alcohol and acetone or by extraction by liquid ammonia.

"7. Nine hours' boiling of the active material with alcoholic sodium hydroxide still leaves considerable potency in the non-saponifiable fraction.

"8. The activity was lost completely after boiling with alcoholic sodium hydroxide for eighteen hours."

Using as a test method spermatomobility tests which depend upon extending the life of the spermatozoon in the isolated epididymis, Moore and McGee (4) proved that these extracts are also effective in mammals (guinea pigs). Funk, Harrow and Lejwa obtained their most potent male hormone preparations from the urine of young men although the testicle extracts also gave definite results. They were led to make use of this source for the hormone by the finding of the hormone in the blood of male cocks by Pezard.

"It seems logical to conclude that since the male hormone is in the blood it would probably also be found in the urine."

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Frank and his associates had also shown the presence of the female sex hormone in the urine.

Funk, Harrow and Lejwa give some interesting though inconclusive data on the relationship of the male and female hormone in capons. "It does seem, however, as if in well castrated animals the male and female hormone may act antagonistically, at least in so far as secondary sex characters are concerned."

Some of the chemical characteristics of the male and female hormone are very similar. "It was now shown that what is true of the female hormone is true of the male hormone: both form alkali salts which are largely soluble in ether."

The specificity of the substance extracted from the testes was determined by Gallagher (5). Extracts of brain, ovary, pancreas, prostate, thyroid, suprarenal, kidney, liver and seminal vesicles failed to give any activity when prepared by the method used in obtaining active extracts from the testes.

In considering the sex hormones, the highly important hormone of the anterior pituitary must also be included. Evans (6) and Evans and Simpson (7) have clearly shown the presence of this hormone.

"Two hormones are secreted by the pars anterior of the mammalian hypophysis, one required for normal growth and the other for normal development of the gonads, thyroid and suprarenal cortex. As regards its effect on the sexual system, the second hormone can be completely nullified by simultaneous administration of the first — the growth substance. Evidently nature has provided the necessary nice adjustment in the relative amounts of the two substances secreted. That the growth of the animal is usually accomplished before the attainment of sexual maturity may therefore plausibly be due solely to the early predominance of the growth hormone."

The sex hormone of the anterior pituitary may be recovered from the urine and is active in both male and female. In further work on the male testicular hormone, if urine is used as a source, the hormone of the anterior pituitary will have to be carefully excluded.

But all of these results, striking as they are, must be surveyed critically and the limitation of this or any method of "rejuvenation" clearly recognized.

It is entirely possible to stimulate the deficient physiological mechanism (including the sexual) to greater temporary activity. Under competent medical supervision such results are frequently desirable but there are dangers and the stimulation, therefore, should not be too great for the structurally weakened organism. The limitations of this type of therapy are well given by Peritz (8).

"If one takes note of this rejuvenation, one must say even in the case of the animal, that not a total but only a partial rejuvenation occurs. Only in quite fixed domains is the function increased. In the human being it asserts itself more strongly. Man lives under altogether different conditions in the struggle for existence, from the animal, and is, accordingly, exposed to altogether different dangers; which above all things involve also the nervous system, and the nerves which regulate the various internal organs, in particular the heart. Moreover, man, because of the finer manner of reaction of his nervous system also uses stimulants, such as coffee, nicotin, alcohol. The injuries which are effected by these stimulants have nothing to do with old age, can consequently also not be set aside by a rejuvenation. On the contrary, it is even to be feared that individuals in whom the heart or circulatory system has suffered, will be injured by the rejuvenation, since now the renewed energy and joy of living will overwork the already diseased tissue still more and thus lead to a more speedy exhaustion of it.

"One must also not imagine that possibly through a rejuvenation the intellect will be increased, since if one wishes to think in rough organic terms, the intellect is dependent upon

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the number of ganglion cells, the communication of these ganglion cells among themselves and the physicochemical processes in them. The sex gland hormone has, so far as known up to the present, only a stimulating action and the task of hastening the course of psychic processes. There will, accordingly, be no improvement if the sex gland hormones light on an old brain, since a part of the ganglion cells is destroyed and this abolition of function can not be set aside.

"Nothing is as yet known concerning a prolongation of life through transplantation of the sex glands. If one desired to demonstrate this in the animal it would be necessary to observe many generations of animals, and moreover, a great number of control animals in which no rejuvenation had been undertaken and just as great a number of animals which had been rejuvenated. Both groups would have to be of the same origin and under similar conditions. The time which has elapsed since the application of this method is much too short to allow of a decision concerning the animals.

"In man the situation is much more unfavorable. The transplantation has been undertaken only in isolated individuals. Their constitution is not known, the lesions are also not known which disease and struggle for existence have inflicted on their constitution. How can one tell whether their lives have been prolonged! It is, however, probable that a prolongation of life has not occurred through it, since death from old age rests on the fact that the hereditary substance which the individual cells of individual organs have received, is gradually consumed. The product furnished by the sex glands, however, merely represents a stimulant and not a substitute for destroyed and consumed cellular elements."

A true rejuvenation is impossible under the conception of a slow structural metaplasia of one tissue to another. Youth could only be maintained by preventing those unknown factors in the vital processes which slowly change the character of the tissues themselves. Many of the functions of the body are controlled wholly or in part by the several hormones; particularly is this true of the purely vegetative, vital processes. In the aging process, however, the endocrine tissues themselves are subject to the retrograde changes which result in progressive functional inefficiency.

In the testes old age gives rise to smaller testes, a result of atrophy of active secreting tissue or of fibrosis. The spermatogenic cells as a rule are the first to be affected and the interstitial tissue outlasts it. In old age, therefore, sex desire (persisting as an established psychic reaction) and sexual ability may persist long after the production of spermatozoa has ceased.

In its broader sense rejuvenation depends not only on the hormones of the sex glands but also, as pointed out by Leschke and others, on several of the glands of internal secretion. Particularly important are the pituitary (anterior) and the thyroid. Again certain substances (vitamins) taken in the food are necessary. Evans and Bishop (9) have shown that a diet sufficing to maintain animals in perfect health may still leave them sterile and incapable of reproduction. The vitamin is apparently a special one and not identifiable as one of the known vitamins necessary for other physiological functions.

So far as sexual ability is concerned however, the influence of diet and vitamins is doubtless not important. The vitamin of Evans and the diets described by Macomber in connection with fertility are important however, in the maintenance of the fertility characteristic of young animals and therefore should be considered in rejuvenation.

Rejuvenation in its broader aspects is impossible. Hygienic measures, moderation in food, alcohol, tobacco, exercise and stimulants, the use of endocrine products (pharmoglandular) and proper diet all contribute to the maintenance of a youthful mind and body with the later decades of life.

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The direct increase of activity of the sexual system may be successfully attempted with those hormones which normally control their functions. There can no longer be any doubt that several hormones are necessary. Certainly the active sexual hormone of the testis and anterior pituitary are required. Thyroid would appear to be valuable even though a specific sex effect has not been shown. Thyroid maintains a normal metabolic rate and gives added energy output, necessary in any effort to restore general body efficiency. These substances may all be given orally. It is interesting to note that Funk, Harrow and Lejwa found that "It would seem, from the results here recorded, that the activity of the male hormone does not entirely disappear when given by mouth. It also appears that testicular extracts, like urine extracts, are active although the comparative activities of these two extracts have yet to be determined." With a proper and potent preparation of this type, rejuvenation of the sexual function is possible. It is not, however, a therapy to be uncritically applied: certainly the laity should not attempt self-medication. Careful medical attention is necessary to determine whether a case is suitable for treatment and to prevent accidents from arising in those in which the general physical condition may be sufficiently below par to undergo excessive functional activity of a particular physiological mechanism.

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Clinical Observations concerning Respiratory Basal Metabolism

(Translated from the article by Prof. F. de Quervain and Dr. F. Pedotti, First Assistant Physician at the Surgical Clinic, Berne.)

(*Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 39 : 646, 1926.)

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AFTER the importance of the thyroid gland for the metabolism of gases, and thereby for the respiratory basal metabolism, had been demonstrated by means of physiological experiment and numerous clinical observations, we were concerned with the problem of investigating, in one class of Basedow patients, in material consisting of

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common goiter bearers and cretins, in order to determine what relationship exists between the clinical estimation of thyroid gland function and the basal metabolism.

Further attempts were made to determine, within the limits of our observational material, what other pathological conditions, not primarily connected with the thyroid gland function, would likewise influence basal metabolism.

An additional problem was that of tracing the relationship between basal metabolism, respiratory quotient, pulse frequency and volume per minute of breath. The point was mainly, to determine whether this relationship — at least in the case of disturbances of thyroid gland function — would permit the estimation of the basal metabolism without the circuitous method of the determination of the consumption of oxygen.

Finally it remained for us to test the relationship (investigated in an earlier work by Dr. Pedotti and Dr. Branovacky) between basal metabolism and deficiency in the Asher-Streuli rat experiments from goiter bearers of various kinds, on a somewhat larger material.

Since we see in the gas metabolism method the first, and up to the present the sole possibility of determining numerically the function of the thyroid gland, or at least *one* component of it, we were concerned with obtaining not merely approximate values. We did not content ourselves with the simple determination of absorbed oxygen, but used a carefully constructed Tissot apparatus, according to our reports, obtained from the Stoppani Company, which had carefully counterbalanced bell weight and water valves sealed with liquid paraffin, and which proved very satisfactory. The air of respiration was submitted to a total gas analysis and in the majority of cases three analyses were made for each experiment.

The calculation of metabolism under 17 years was based on the standard values of Benedict, for adults on those of du Bois, using the formulae and tabular material worked out by Boothby and Sandiford in the Mayo Clinic (1). The experimental procedure was briefly as follows:

On the evening before, between 6 and 7 o'clock, a light meal, on the day of the experiment, an empty stomach, with avoidance of bodily exertion and much walking. (Patients not residing at the clinic must be brought to the laboratory in a conveyance.)

First, comfortable resting in bed, undressed except for underclothing, until pulse and breathing had become entirely regular. Then a preliminary experiment with controls of pulse and breathing and calculation of the volume per minute. Then the main experiment. If the volumes per minute of both determinations varied greatly, the experiment was not valid and had to be done over. It is important that with timid patients, the experimental room should not cause excitement. For this reason we cut off the patient's view of the apparatus with a curtain. The personnel must understand that they are to work silently through the entire procedure. The importance of absolute muscular quiescence has been demonstrated again in the latest control experiments of Benedict. If there is failure on this score the entire accuracy of the gas analysis is not valid.

In the following a series of 178 cases will be reported, of which 42 cases were hyperthyroid, 52 cases had common goiter and 47 cases cretinism with and without goiter. Then there are 34 cases of various illnesses, in which the thyroid gland is not ostensibly or particularly associated. The percentage of

1. In a recent communication (1925) Benedict draws attention to the fact that the American standard values for women are about 5 per cent too high. Nevertheless, since our Swiss values agree fairly well, it shows above all, that the B.M. determination in individuals who are not trained to the method by a large number of tests, as a rule results in values a little too high, because it is almost impossible to induce absolute muscular quiescence in patients. This error is practically constant in all our determinations of gas metabolism; having heeded all known precautions, however, this amounts to only a few per cent.

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individual goiter forms does not agree with that of our clinically observed material for the reason that gas metabolism experiments were done on only a part of the goiter individuals without clinical disturbance of function and because a good portion of the cretins were not successful for the experiments by reason of their mental deficiency.

From the investigation it was concluded, particularly in those cases where there was tracheal stenosis, that quiet regular breathing was impossible for the calculation of the basal metabolism.

We shall now report the results in accordance with the various viewpoints mentioned above.

I. Basal Metabolism and Clinical Findings

1. Average Values of the Individual Groups

We begin by assembling the average values of the individual groups and by investigating what causes the important deviations from the group median in individual cases. We note that the connection of the isolated cases to the functional groups had been assumed exclusively on the basis of *clinical* symptoms and *not* on the basis of gas metabolism experiments, for it was a problem of testing the importance of the latter for the functional analysis.

Table 1. Survey Table concerning the Composition and the Average Values of the Groups

Groups	Pulse frequency	Volume per minute	R. Q.	Basal metabolism in %	No. of cases
1. Basedow goiter before treatment	109	7.6	0.73	+35.9	42
2. Common goiter	80	5.7	0.78	−0.6	52
3. Cretinism with goiter	68	6.0	0.83	−8.0	32
4. Cretinism without goiter	78	4.7	0.84	−11.4	9
5. Operated Basedow and other goiters (excl. the control experiments from Groups 1-3)	71	5.2	0.75	−7.5	9
6. Diverse cases	77	5.8	0.76	+2.4	34
				Total	178
				Control experiments	68
				Total number of experiments	246

From the above survey table it is evident that the group of cases clinically designated as *hyperthyroid*, on the average, show the highest pulse rate, the highest volume per minute and, with +35.9 per cent, the highest basal metabolism and yet the lowest respiratory quotient.

The instances with no clinically recognized disturbance of function, that is *euthyroid goiter*, show normal median values all along the line, with a basal metabolism of −0.6 per cent.

Goiter associated with symptoms of *cretinism* (including the border cases) shows an average basal metabolism of about −8 per cent, with normal volume of breath, slow pulse and a respiratory quotient higher than that of the above mentioned group, *i. e.* 0.83.

Cretins without goiter show a still lower basal metabolism: −11.4 per cent with minimal volume of breath and a respiratory quotient somewhat higher than the foregoing groups, namely 0.84.

The *group of diverse cases*, which require special mention, show an average metabolism of +2.4 per cent, with pulse frequency, volume of breath and respiratory quotient functioning in normal values.

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The values obtained for the first four groups show in the arithmetical mean, an important gradation from Basedow goiter down to cretins without goiter. The relationship between the clinical picture and the gas metabolism will be still more striking if one considers the graphic table and thereby the distribution.

Table 2. Clinical Thyroid Gland Function and Basal Metabolism. All Thyroid Gland Cases (As in All the following Tables excepting Tables 3 and 11)

0

Groups	± 30-39	± 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-r Basal metabolism %
Basedow goiter (hyperthyroidism)					· · ·	· · · · · · · ·	· · · · · · · · · · · ·	· · · · ·	· · · · · ·	· · ·	·	· ·	· ·	·
Goiter without functional disturbance (euthyroidism)			· · · · · · · · ·	· ·	· ·	·	·							
Cretins with goiter	· ·	· · ·	· · · · · · · · ·	· · · · · · · · · · · · · · · · · · ·

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results confirm the facts already known, so that it is superfluous to linger over them. The rather low basal metabolic rates, even in cases of severe Basedow, in agreement with numerous reports in the literature, rest in part on the careful consideration and avoidance of all those things which can increase the metabolism. Elimination of masks, least possible disturbance, ample tube connections, easily functioning valves, careful counterbalancing of the spirometer bell are factors of importance which intelligent patients will soon recognize if they have once been tested with a poorly functioning apparatus.

Only three cases in which the gas metabolism lay in the realm of normality, *i. e.* under +10 per cent, deserve mention.

1. Z. E., 28 years old, female. Possessed a nodular goiter for years, for the previous month slight basedowification, *i. e.* appearance of heart palpitation, insomnia, tremor, exophthalmos, B. M.+9.4 per cent. Histological: Struma nodosa parenchymatosa microfollicularis.

2. R. N., 36 years old, female. Treated for 5 years for slight Basedow. Slightly diffuse and nodular struma. Acceleration of pulse, some tremor, no exophthalmos. Diagnosis questionable, nevertheless, "forme fruste." B. M.+7.5 per cent. Histological: Struma nodosa parenchymatosa.

3. St. M., 30 years old, female. Nervousness. Treated for two years as a slight Basedow case. Still in a quiescent phase. No definite clinical aspect. B. M.+4.6 per cent. Histological: Slightly diffuse Basedow changes.

In all three cases the Basedow symptoms were so slight that the diagnosis seemed questionable, and a low basal metabolism was to be expected.

3. The Common Goiter

The Goiter without Functional Disturbance of the Thyroid Gland

The cases in this category oscillate so closely around the null line that their average value of −0.6 practically is equal to 0 per cent. Only seven cases overstep the ±10 per cent limit, some above and some below, with limiting values of −14 per cent and +15 per cent. Pulse, volume per minute and respiratory quotient congregate, however, around the average value, with a fairly slight distribution. The three values combine in such a variable manner in an individual that it is impossible to draw any conclusion as to the basal metabolism from one of them, or from pulse and volume per minute combined.

Concerning the significance of the ±10 per cent excessive values, the following may be said:

Values from −11 to −15 per cent were found six times. In none of these cases was there any clinical sign of under-functioning of the thyroid gland or any stigmata of cretinism. From a purely *clinical* standpoint, the matter does not concern the border cases of the latter. Besides, a short preliminary control experiment twice gave normal values, namely −1.3 per cent instead of −11 per cent and −10 per cent instead of −15 per cent. Histologically, in the five operated cases, various types of goiter were found, alone and in combination: Struma colloides diffusa, colloides nodosa, parenchymatosa nodosa. Either we must agree that in these patients a clinically latent, relatively temporary underfunctioning occurred, or we must, with Benedict himself, incidentally, extend the limits of the "normal" under the ±10 per cent.

Twice, values of more than +10 per cent were found, namely once, 13 per cent and once, 20 per cent. In both cases dyspnea occurred, in the one case (+20 per cent) nervousness also without any other Basedow symptom. We must abandon the attempt to determine whether the high value for the basal metabolism is traceable to the dyspnea or whether one must account it as a casual occurrence. The latter assumption is more acceptable for the +13 per cent than for the value of +20 per cent.

One point must be emphasized, namely

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that the histological condition of the goiter appears to play no part in these deviations from the average. After the rat experiments we must agree that the colloid strumæ are as active as the parenchymatous small follicular strumæ. This is also recognizable in the investigation of the thyroid gland venous blood, which proves no more active than the blood of the general circulation. Therefore, the question may be posed whether the high basal metabolic values in ordinary strumæ chiefly affect colloid strumæ. We find in 15 cases of genuine colloid strumæ an average value of +0.6 per cent, such an insignificant difference as compared with the median of the group that we have to negative this question *for our material*. This does not exclude the fact that, in other regions with greater Basedow frequency (for example Norway, and according to Holst), colloid goiter can not give higher values. The same applies to the border cases of Basedow (Basedow distribution according to Hellwig, Breitner, latent thyrotoxicosis according to Holst). We must hence straightway assume a varied activity for colloid struma with regard to the geographic distribution.

4. Cretinism with Goiter

Here, for the first time, the differentiation between the gas metabolism investigations on cretins with goiter and the investigations on cretins without goiter is encountered (2). While the disease picture in cretins with atrophic thyroid glands, *without* goiter, is so typical that there can be no doubt as to its identity, the state of affairs is different with cretins *with* goiter. We find here an indefinite transition from euthyroid goiter bearers to cretins with goiter, and it is often only a matter of opinion whether one wishes to accept a certain degree of dullness, an unobtrusive lack of intelligence, slight speech defect, a little deafness as a slight degree of cretinism or not. The principle diagnosis is so simple that we observe these constitutions progressing towards the other side, without sharply defined borders, to the worst forms of cretinism in which the diagnosis is not at all intricate. That the border cases trending towards euthyroidism show a normal gas metabolism is not to be wondered at if we assume the extended limits which must be recognized as "normal." Let us look at the following clinical cases of cretinism with plus values:

1. B. C., 14 years, male cretin. Conglomerate goiter, with difficulty in breathing. Very moderate intelligence. Suggesting hypothyroid constitution, without pronounced stigmata. B. M. +1.3 per cent. Histological: Struma nodosa parenchymatosa microfollicularis.

2. B. M., 14 years, female, moderate intelligence. Underdeveloped bodily. Cretinoid constitution. B. M. +1.0 per cent. Histological: Struma nodosa colloides.

3. D. M., 24 years, female. Nodular goiter with dyspnea. Nervous, excited, yet apparently cretinoid. B. M. +3.6 per cent. Histological: Struma nodosa colloides.

4. H. Chr., 27 years, male, deaf, cretinoid constitution. B. M. +7 per cent. Histological: Struma nodosa parenchymatosa et cystica.

5. L. E., 42 years, female. Rapidly developing nodular goiter, left. Right, atrophic thyroid gland. Slight difficulty in breathing. Pronounced cretinoid constitution. 140 cm. high. Little intelligence. B. M. +1.6 per cent (−9.6 per cent post op.). Histological: Proliferating struma according to Langhans.

6. E. A., 64 years, female. Nodule conglomerate. Dyspnea. Total cretin. 147 cm. high. B. M. +13.17 per cent. Histological: Struma nodosa colloides partim cretacea.

7. B. E., 46 years, female. Deaf and dumb cretin with constricting goiter. B. M. +6.5 per cent. Could not be brought to quiet breathing.

The first four cases are cretins of less severe degrees, still capable of being educated. Dyspnea was twice observed, once excitability, both factors capable of increasing the

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B. M. In the fifth case there was a badly degenerated nodular goiter, after its removal the B. M. dropped to −9.6 per cent. The sixth and seventh cases concern total cretins with the expected impossibility of obtaining complete quiescence for the investigation. If we say that *Degree of Cretinism I* = slight and *Degree of Cretinism III* = worst, in connection with the *metabolism* of goiter-bearing cretins, the accompanying table is the result.

Table 3. Degree of Cretinism and Basal Metabolism

0

Degree of cretinism	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29
I. (23 cases)	·	·	· · · · · · · · ·	· · · · · · · ·	· · · ·		Basal metabolism %
II. (5 cases)	· ·			· ·	· ·		
III. (3 cases)				·	·	·	

0

From this table it is evident that with cases easy to experiment on, hence the greater number of cases (about ¾) forming our statistics on cretins of the first degree, we find all gradations of gas metabolism from +9 to −39, yet in *ca.* 5/6 of the cases there are values under 0, *i. e.* under the normal average. The gas metabolism in this degree of cretinism is generally depressed, yet additional insignificant circumstances can bring it, at least transiently, to the normal height. The gas metabolism experiment appears to be less a criterium in these border cases than the general clinical observation. The more severe the cretinism, the smaller the proportion of cases accessible for metabolic investigation. From our cases of Degree III most must be eliminated from the experiment. In the three cases represented in the table the experiment could be done only with great difficulty.

(*To be continued*)

Practical Therapeutics

Pancreas Enzymes in Local Treatment

ADVANTAGE may be taken of the action of the proteolytic enzyme trypsin as a local application. Its capacity to digest the protein of dead tissues is extraordinary and inasmuch as little use has been made of pancreatin in medicine, even as an agent in digestive disturbances, physicians generally are not fully appreciative of the powerful character of its action. In the manufacture of pancreatin in the G. W. Carnrick Co. factory workers frequently develop bleeding from the fingers, palms of the hand, the nose, etc., and examination of these sites discloses that the light pancreatin powder settling on the moist surfaces has digested all

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dead epidermis and leaves the living dermis exposed. The U. S. Pharmacopoeia prescribes no standard for strength of trypsin in pancreatin; it fixes only the amylolytic activity. There is, therefore, some variation in the trypsin activity of commercial pancreatins, and salves or ointments made up containing pancreatin for local application should be used cautiously until the strength has been determined.

Uses of this kind — furuncle, acne vulgaris, eczema seborrhoicum, cicatrices, indolent indurated ulcer edges, etc., are described in the abstracts of articles by Axmann, Kuhn and Bassmann (below). Such pastes, in view of their definite activity, under careful supervision, should find a useful place in practice.

Concerning Cosmetic Treatment of Cicatrices with Pancreas Salve. — Axmann. (*Med. Klin.*, **24**: 67, 1928.)

Cicatricial distortions following surgical wounds often spoil the otherwise good results, to say nothing of the cords of the cheloids as thick as a finger as they are occasionally to be seen in severe, healed, old lupus foci. And yet here this may be quite satisfactorily prevented if one proceeds with necessary perseverance. Following a preliminary treatment with poultices of pepsin-hydrochloric acid for the purpose of softening, the cicatricial tissue is vigorously rubbed in with pancreas salve and massaged with the adjuvant of electrical vibrations. There may possibly be a too great skin irritation following this treatment, and this may again be equalized by boracic ointment or powder. Through this simple procedure, carried out for months with great perseverance, extensive cicatricial fields in addition to cicatricial cords almost as thick as a finger, especially on the face and extremities where they frequently impede movement, are brought to the vanishing point (the patient may himself accomplish the treatment). The pancreas salve appears to develop an especially profound effect, which as is self-evident, appears also of importance for suppurating wound surfaces.

Concerning Treatment with Pancreas Enzymes. — Kuhn. (*Münch. med. Wochenschr.*, **75**: 289, 1928.)

The great advantage of enzyme ointment and of enzyme powder lies in the fact that they do not attack or irritate the healthy tissue in any way. They merely liquefy the necrotic tissue and digest pathologic products of the skin and mucosa. The excellent results which the author has obtained for years with pancreas enzyme preparations, are shown in the following diseases:

(1) Suppurative wounds. In particular wounds which arise through cauterization with chemically impure acids in the metal industry and show a poor healing tendency in general, heal up smoothly within a few days under enzyme ointment dressing. Suppurated insect bites also, which show a solid scab following opening of the pustule, which was not to be influenced either by bathing or indifferent ointments, were healed in a very short time by pancreas enzyme.

(2) Furuncles, which were treated with enzyme ointment, healed so well that the author considered incision therapy as superfluous.

(3) Acne vulgaris. The pustules dried up very soon. Anointing of the face before retiring, without bandage, sufficed for the patient to be able to gently remove the scurf digested by the enzyme by washing on the next morning.

(4) Eczema seborrhoicum. The treatment takes longer, but the evening inunction also suffices in these cases and a light protective dressing in which the entire absence of irritation of the enzyme ointment against the healthy skin must be stressed as a great advantage.

(5) Rhinitis anterior. The adhering crusts are very easily softened by the ointment, so that they can be removed without pain.

Since the patient's ability to return to his work is hastened by the more rapid healing, the treatment with enzyme preparations is to be recommended in industrial practice.

Experiences with Roehm's Wound Ointment and Wound Dusting-Powder in the Treatment of Wounds. — Bassmann. (*Therap. Gegenw.*, **69**: 93, 1928.)

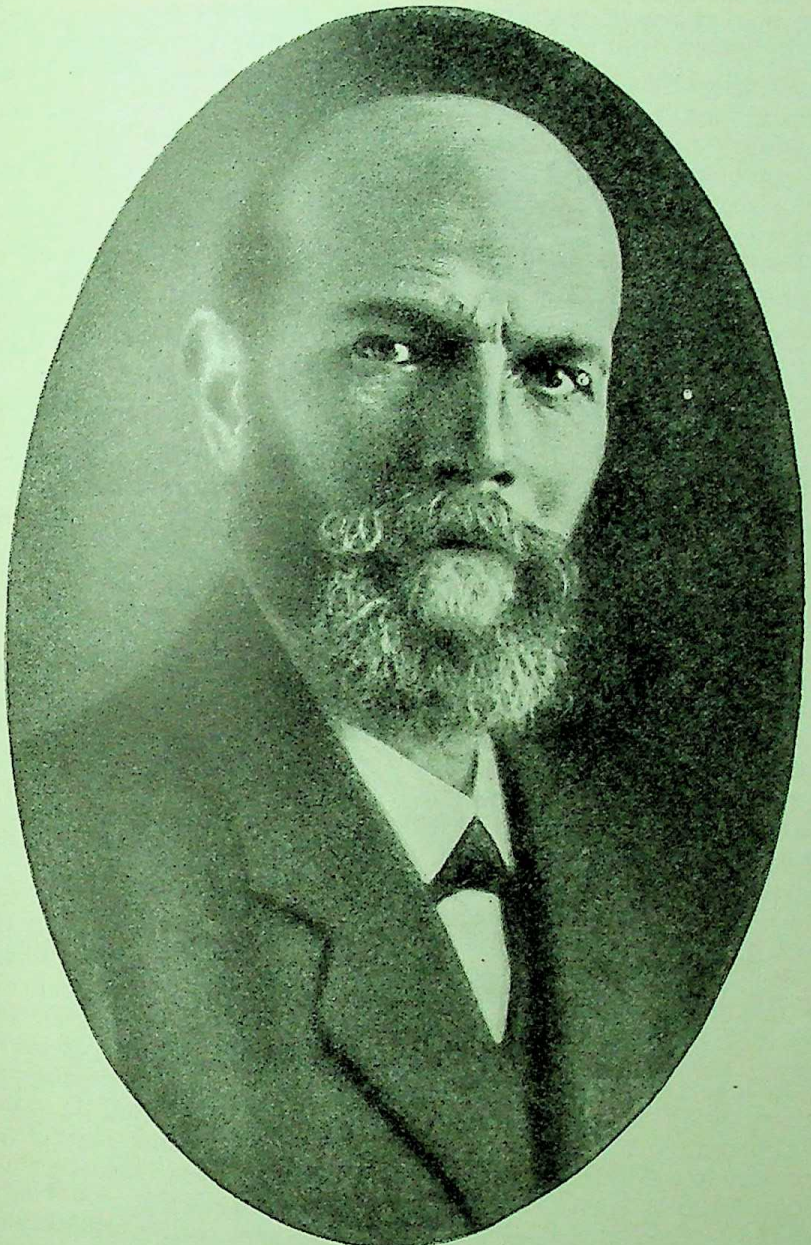
Roehm's wound dusting-powder and wound ointment consist of extract. pancreat., Zinc. oxydat. and Vasel. flav. or Talc. venol. The most important ingredient is, to be sure, pancreat. extract, which owing to its fermentative action, in particular that of trypsin, and also of the other constituents of pancreas secretion, aids the tissue in its work of cleansing wounds. Pancreas secretion through its

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The Doctor's Page



JOHANNES VON KRIES

(1853-1929)

To classify Johannes von Kries under the caption of one special line of endeavor is impossible, for he is associated with contributions to physiology to physics in conjunction with his physiological work and to psychology which appears to have developed out of these two studies. Mathematics, of course, formed the basis of these studies, and his bent for this subject was early displayed in "Principles of Calculus" published in 1886.

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This is still considered a classic and has a second edition published in 1927. Logic and philosophy have also received the attention of this unique individual. His interpretations and grasp of the thoughts of both Goethe and Kant are still the subject of much favorable comment.

Among German scientists von Kries is considered primarily a physiologist, for that was not only his life's work but also the subject in which he gave instruction for years. The rank of doctor rests both on his having qualified in the state examination (1874-1875), and on his excellent studies concerning the blood, the measurement of its flow, the activity of the heart and pulse, and particularly the work on the muscular and nervous systems.

Von Kries was born October 6, 1853, in the picturesquely fortified town of Graudenz on the Vistula River (now the Polish Grudziadz). His youth appears to have been a pleasant, unassuming period in which he was occupied with studies at the gymnasium at Marienwerder (1865-1869). His university studies were distributed between Halle, Leipzig and Zürich; he also attended the physiological institutions of Hermann von Helmholtz and Carl Ludwig, both of whom were inspirations and guides in his work at the laboratory, and in subsequent years. In 1880 he was installed as Professor of Physiology at the University of Freiburg. It was in this capacity that he laid the ground work for the "duplicity" theory of vision (rod and cone principles). In fact ophthalmology is much in debt to von Kries for the solutions of many intricate problems (for example, color blindness which he termed protanopia (red-blindness) and deuteranopia (green-blindness) and for instruments (such as Nagel's anomaloscope) without which this branch of science would be greatly impoverished. In 1881 he married, happily. (From this union there were four children; the oldest married the physiologist Nagel.) Besides the titular honors of *Hof-Rat* and *Geheimer-Rat* he had the distinction of being called to posts in Leipzig (1895), in Berlin (1897) and in Munich (1908).

Von Kries was fitted particularly to pursue the rôle he chose, for he had a faculty of interpreting the contributions of both predecessors and contemporaries, for conveying his interpretations in a clear manner and for carrying forward to still more complete results the intricate problems of such profound thinkers as, for example, von Helmholtz. Though the insidious malady from which von Kries suffered for years sometimes made the fulfillment of his tasks almost impossible, yet he never avoided even the smallest of his duties until absolutely forced. Only with the cessation of life (December 30, 1929) was von Kries released from the terrific combat between the desire to push forward his chosen work and the disease which was constantly undermining his powers.

Of his numerous works on physiology the most important is "General Sense Physiology." As early as 1891 von Kries contributed with a treatise "Concerning the Relationship between Physics and Physiology" in which he displays his ability in both subjects. A rectorate address in 1898 was entitled "Concerning Sense Perception," and there followed later (1901) an excellent study "Concerning the Material Basis of Consciousness." It is easy to observe how his thought processes actually were progressing away from pure physiology to its more abstract applications namely psychology, and kept advancing until a culmination in 1916 with the magnificent work on "Logic." This, according to W. Trendelenburg, his pupil, was "a fountain of information" concerning the science of nature, of the mind and of some of the most important and most intricate problems of perception, presented by one whose keen mind "could well nigh push on to the very limits of knowledge."

In the realm of physics von Kries, like von Helmholtz, was interested in sound and presented in 1892 (*Zeitschr. Physiol.*) a treatise on "Absolute Sound," which added to his illustrious name still further honors. Carrying these principles further, in his characteristic way, he gave us a monograph entitled "What is Musical," which is considered the best essay on the physiology of music since that of Albert Billroth, with the same title. Furthering the studies of von Helmholtz concerning light, von Kries collaborated not only in editing but also in contributing in *Handbuch d. Physiol. Optik* (Handbook of Physiological Optics) especially with an article concerning the "Laws of Sight Perception of H. Helmholtz."

In yet another field of study did von Kries distinguish himself, namely that of Philosophy. The careful penetration of the

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Medical Subjects by Famous Masters



"THE DOCTOR'S VISIT," by Jacob Toorenvliet (1641-1719)
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Editorial Comment

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Menstruation, the Sex Hormone and the Renal Threshold

KNOWLEDGE of the menstrual process and of the female sex hormone has increased enormously in the past 10 years. Among those who have contributed the group at Mount Sinai Hospital, New York, headed by Robert T. Frank stands in the very front. Their contributions have been fundamental, original and scientifically sound. The demonstration of the active hormone in the blood and in the urine with the development of a technique for isolating it has been particularly enlightening. Very recently (1) Frank, in collaboration with one of his best known associates in this work, Morris A. Goldberger, has still further extended our knowledge of the relationship between the hormone in the blood and urine and the menstrual process and its abnormalities. Frank had previously shown that in normal women free from menstrual disturbance there is in the great majority of cases a definite increase in the concentration of the female sex hormone in the blood during the 10 day period just preceding menstruation. Just before or at the time of menstruation the hormone practically disappears from the blood and in non-pregnant women from 4 to 10 mouse units of the hormone appear in the urine in 24 hours beginning about 5 days before menstruation and reaching the acme immediately before menstruation. In menstruating sterile women (husbands potent) free from inflammatory disease and with no obstruction of the tubes twenty-nine tests made during the 10 day period preceding menstruation showed only one positive, whereas in a group of forty-six normal women thirty-two, or 69.5 per cent were positive, and in those functionally sterile only 3.4 per cent were positive.

In a large number of amenorrheic women two groups were distinguished by means of the blood and urine test. In the first, no cyclic accumulation of sex hormone can be demonstrated. In the second, an accumulation of hormone in the blood can be demonstrated in distinctly diminished amount.

"These observations warrant the deduction that the amount of female sex hormone produced is not necessarily an accurate index of the quantitative effects to be expected. The effect produced will depend on at least three factors: (1) the amount secreted, (2) the rapidity with which the hormone is utilized or fixed in the genital tract (as previously mentioned, it is as yet unknown whether during its utilization the hormone is fixed in the genital tract, utilized and then excreted or destroyed); (3) the rate and level (threshold) at which the excretion takes place.

"To recapitulate, we have noted that, particularly in the sterile and amenorrheic groups, the renal threshold (perhaps also the intestinal threshold, which has not yet been studied in these cases) is persistently and

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recognizably lowered. The hormone appears to be excreted with sufficient rapidity and in such amount as to cause a reduction of its concentration in the circulating blood. Consequently, in spite of functioning ovaries, little effect on the sex tract is produced. In the one group, amenorrhea with comparative lack of uterine function is noted; in the other, sterility due to insufficient pregravid (premenstrual) uterine reaction results."

The idea developed by Frank and Goldberger relative to renal permeability for hormones and the possibility of a lowering of the threshold sufficient to prevent the normal action of these hormones is a very practical one. In such a cyclic physiological phenomenon as menstruation which depends upon the attainment of a certain maximum concentration of hormone the effect of lowered renal permeability preventing such concentration is obvious. It seems possible, also, that the idea might easily be extended to other hormones which are slowly elaborated in small quantities during the 24 hour period. Constant removal by the kidneys of thyroid hormone from the blood might conceivably result in hypothyroid symptoms and consequent compensatory enlargement of the thyroid gland. Frank and Goldberger state that there is some evidence of such a reduction of the hormone level of the anterior pituitary, which appears in the urine and they say:

"On the basis of these observations, with all due reserve, we propound the query whether not only the female sex hormone and pituitary hormone but also other internal secretions may be excreted by the kidneys and other emunctories. If this hypothesis obtains, a balance between the amount secreted, utilized and excreted must be drawn in every instance to evaluate the physiologic effects to be looked for, as well as to govern the dosage in organotherapy."

The demonstrated existence of a changeable renal threshold for sex hormone opens up a promising field of research. The therapy of endocrine diseases and the use of endocrine products in medicine might undergo marked change if variations in hormones are due not to defects of elaboration but to variations in the capacity of the kidney to retain them.

1. Frank, R. T., and Goldberger, M. A., *J. Am. Med. Assn.*, 94, 1197, Apr. 19, 1930.

Abstracts

Severe Case of Diabetes Improved by the Administration of Salts of Nickel and Cobalt Simultaneously with Insulin.— Roch and A. duBois. (*Bull. et Mém. Soc. méd. Hôp. Paris*, **45** : 412, 1929.)

Up to the present only in cases of relatively slight degrees of diabetes were results obtained with the administration of nickel and cobalt, while in more severe cases this therapy remained unsuccessful.

The author observed a severe case of diabetes in which, during 24 days of insulin therapy coincidently 20 gr. of nickel chloride and cobalt chloride in solution, each 0.04 gr. in 100 parts of water, was given twice daily with very pronounced results. The condition of the patient 8 days after the commencement of this therapy was very much improved and lasted for many months. It would naturally be of practical value, if by means of small doses of nickel and cobalt, the use of insulin might be modified in the diabetic without any resulting harmful effect on the organism.

Communications on the Activity of the Hormone of the Anterior Lobe of the Pituitary. — Max Reiss and Käthe Langendorf. (*Endokrinologie*, **3** : 161, 1929.)

According to the authors' investigations the sex hormone of the anterior lobe of the pituitary acts on the genital system of female dogs and rabbits, producing changes similar to those already observed in rats and mice.

The corpora lutea maturing under the

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action of the anterior lobe hormone are genuine corpora lutea ("epitheliala"). The hormone of the anterior lobe of the pituitary affects cholesterin metabolism of normal female rabbits and dogs, so as to increase blood cholesterin. The increase comes about indirectly through the ovary. In ovariectomized animals the increase does not occur, it is lacking if there is no follicle in the ovary.

A definite effect of pituitrin on blood cholesterin could not be determined.

Concerning the Influence of the Anterior Lobe Hormone on the Respiratory Metabolism of Rabbits. — Max Reiss and Anton Winter. (*Endokrinologie*, **3** : 174, 1929.)

The authors injected doses of hormone between 200 and 4000 mouse units, in which the mouse units consisted of the smallest amounts that were able to bring forth follicular ripening and ejection into the ovary, hypertrophy of the uterus and stratum, within 100 hours, in the infantile mouse, by means of six injections divided between 2 days. From their investigations the authors could not establish any effect on the respiratory metabolism with any certainty.

Concerning the Manner of Acting of the Thyroid Gland Hormone. — Rudolf Weil. (*Klin. Wochenschr.*, **8** : 652, 1929.)

Tests with synthetic thyroxin (Scherling). Since it was determined that thyroxin itself does not possess a proteolytic property, nor affect the enzymatic splitting-up of albumin *in vitro*, through the direct effect on the ferment, proferment or substrate, the author investigated the course of tissue autolysis after dosage with thyroxin *in vitro*. Hence it was shown that thyroxin in very small amounts affects a quantitative increase of autolysis in guinea pig liver, in neutral reactions, in a dilution of 1:400,000 it causes an increase of over 50 per cent in 24 hours.

This finding only supports the interpretation that thyroxin starts a colloid-chemical change of cell structure, in the sense of an increase of degree of permeability of the marginal surface, which leads either to an improvement in the power of the ferment to attack (through liberation of adsorption agglutinins, increase of spacial dissociation of ferment and substrate), or to a disturbance of the reaction equilibrium (modification of the split products). Both factors depend, however, on the intensity of the enzymatic splitting-up of albumin.

Somatic and Autonomic Innervation. — Leo Hess. (*Wien. klin. Wochenschr.*, 42 : 353, 1929.)

The presentation that in experiment, the hormones adrenalin and hypophysin effect a contrary, constricting or dilatating action, according to the condition of the cell walls of the blood vessels and exercise a reaction process on them, is interesting; correspondingly, the constricting action and the blood pressure effect occasionally fail in human beings.

The autonomic nervous system and its accessory organs prove to be — eventually with the aid of sensibilitizing substances — susceptible to the hormone. On the other hand the production of hormone is regulated by the autonomic nervous impulse. Adrenalin and hypophysin, for example, act not only on the definite nerves but also directly on the smooth musculature of the blood vessels, the ureter, etc. A modification of the somatic innervation by means of the hormone was not ascertained.

Asthma. Pharmacodynamic Treatment of Asthma Symptom Particularly by Means of Adrenalin and Ephedrin. — Zunz. (*Bruxelles méd.*, **9** : 924, 1929.)

Adrenalin is the medium which acts in truly dilating manner on the bronchi. By means of experimental research the activity of adrenalin is measured and it is shown that this is greater the stronger the contraction of the fibers. Ephedrin has an advantage over adrenalin: warm, it is more stable, it does not lose its activity with *per os* administration, and acts, though a little more rapidly, with a more lasting effect than adrenalin. Besides, increase in blood pressure was never observed with ephedrin. It has been shown experimentally that ephedrin acts directly on the nerve fibers, and cure by ephedrin has been cited by several authors.

Contributions to the Biology of Extractive Substances from the Cells and Tissues. — Ferd. Winkler and Franz Köck. (*Zentr. inn. Med.*, **50** : 610, 1929.)

In the course of an undertaking for the purpose of obtaining pure hormone the authors have contributed the following findings:

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1. The extractive substances gave no albumin reaction immediately after they were derived, but after several days there occurred a significant albumin reaction despite sterile preservation.

2. Freshly made preparations are white or light yellow, but darken under the influence of light. Also the original light preparations yield a dark color with Agaricus melleus-tyrosinase in weakly alkaline tyrosine solution.

3. Another extractive substance could be obtained from the female sex glands which differed from that obtained from the male and the extractive substance derived from the ovarian stroma was differentiated from that derived from the corpora lutea. The extractive substance derived from the sex organs exercises not only an entirely stimulating effect on the sex impulse but also induces a definite augmentation of the external genitals. The increase in libido is so great that a male mouse, quite weak, when treated with this hormone in captivity, promptly usurped the sex function.

4. From the heart of animals previously sacrificed after suitable preparation of the musculature according to the method of the authors, an extractive substance was derived which, similar to that of Haberlandt, was able either to quiet the heart or to cause it to beat. The substance obtained by the authors from the liver has not only an insulin effect but also a striking growth promoting effect; this liver substance also has a favorable effect on heart activity.

The extractive substance which was obtained from the tonsils has a stimulating effect on the blood-forming system. The extract from the lymph glands acts likewise. The extractive substance derived from the spleen has besides an influence on the hematopoietic system, another individual effect in the sense of an instigator of blood coagulation and also in the sense of an influence on heart activity. The extractive substance derived from the thymus has a similar effect. An active insulin was derived from the pancreas and with simultaneous extraction of pancreas and brain, an extractive substance which exhibited particularly intensified insulin effect was obtained.

Resistance to Incretion. — W. Falta. (*Wien. med. Wochenschr.*, **79** : 852, 1929.)

In healthy persons Högler and Holler have noted that large amounts of thyroxin do not affect either the basal metabolism or the cardiovascular apparatus. In obesity thyroxin medication is only to be reckoned if the calorie administration is diminished, as Falta shows by diagram. Plummer has contributed that thyroxin in Morbus Basedowi does not act if the basal metabolism has reached about 60 per cent. Observations of Falta and Bauer confirm this assumption. According to Falta's observations the effect is lacking in exogenous thyroxin. The sum total of all observations which have been initiated by pituitrin and insulin, advance the question as to whether the resistance to incretion is not conditioned by a stronger counter-regulation. It is not possible in every case to reduce the effect of the incretion to a simple form.

Concerning Resistance to Incretion. — Jehle. (*Wien. klin. Wochenschr.*, **42** : 823, 1929.)

The slight virulence of large doses of thyroid gland in children suggested the idea that this might chiefly be due to inactive substance. On this ground the excretion of water through the lungs under the influence of thyroid gland was tested. Tests were made on normal children as well as on nephritics and epileptics. The individual experiment on more than a hundred cases has not yet been concluded. It appears that under the influence of thyroid gland medication the water content of inspired air is definitely increased, yet after several weeks it again falls back to normal. From this it may be deduced that in spite of relative non-toxicity, thyroid gland medication is ineffective and perhaps this finding forms the explanation of the fact previously offered by the author, that there may be a process of dehydration in nephritics although neither increase of diuresis nor of sweating could be observed which would clarify the process of dehydration with loss of weight.

Concerning Resistance to Incretion. — W. Falta and F. Högler. (*Wien. klin. Wochenschr.*, **42** : 823, 1929.)

Numerous observations have already been made concerning resistance to incretions, for example, in diabetes insipidus against pituitrin or in diabetes mellitus against insulin. There are also older contributions concerning the resistance to thyroid gland substance, particularly in children and young animals. The authors report on two cases of a high

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degree of resistance to thyroxin in adult individuals (one case of evident lues affecting the brain — a Parkinsonian). This individual was not resistant to thyroxin derived endogenously, since no myxedematous symptoms were evident and the basal metabolism was normal. Entirely analogous observations may be made in the case of resistance of diabetics to insulin. A demonstration of such a case was given. The question of resistance to incretion was seen by the authors to be a counter-regulation chiefly released through the central nervous agency. In the case of diabetes the problem must above all be concerned with a release of suprarenal activity. An analogous circumstance of resistance to thyroxin could be demonstrated in animal experiments.

Concerning Hyperthyrosis and Its Treatment with Micro-Iodin Doses. — Martin Engländer. (*Würzburger Abhandl. Gesamtgeb. Med.*, **6** : 1, 1929.)

The author takes sides with the theory that iodin is the chemical or physical principle present in the thyroid gland hormone. The decreased function can be greatly influenced by means of micro-doses of iodin alone, there is no practical advantage in the repetition of the curves. Apathic persons lacking energy recover under this cure, become anxious to work and are capable. The thyroid gland hormone is the strongest dynamic principle in the sense of a catalyzer. The therapy with micro-doses of iodin differs from thyroid gland therapy in that it does not have the effect of rapid oxidation of fat. The author never observed emaciation with micro-doses of iodin.

Thyroid Gland Tablets in Persons with Hypertonia. — B. Molnar. (*Therap. Gegenw.*, **70** : 191, 1929.)

The author presents the observation on a certain form of high blood pressure, in which thyroid gland tablets were administered with success. Evidently the thyroid gland tablets further oxidation increase and besides act to reduce obesity. In patients with essential hypertonia who suffer from joint edema, there are two symptoms, namely obesity and edema, which give indication for thyroid medication; the third symptom, hypertonia, does not. Nevertheless, the author treated thirteen patients of this sort, with blood pressure up to 210 mm., very cautiously, to be sure, with thyroid gland medication 0.10 gr. ea beginning with ½ tablet and advancing twice a day 1½ tablets). In every case th was decrease in body weight, significant lo ing of the blood pressure and disappeara of the edema. By means of thyroid gla treatment the blood pressure decreases w accounted as intoxication symptoms and such cases the medication is recommende The author never observed any seconda effect which would make cessation of t treatment desirable. It is, of course, com pulsory that dosage be given cautiously.

The Physiology and Pathology of Blood Coagulation. c. Hormone-Coagulation and Gland Function. — Edgar Wöhlisch. (*Ergebn. Physiol.*, **28** : 588, 1929.)

According to the investigations of Cannon and Gray, adrenalin in small doses administered intravenously (0.001 mg. per kg.) a in somewhat larger doses administered sub cutaneously, shortens the coagulation tim to ⅓ the normal value. By means of th extracts of the anterior and posterior lobes of the pituitary the blood coagulation shoul be influenced in the opposite way. Accordin to J. la Barre the coagulation-promotin extract of the posterior lobe considerabl accelerates the formation of thrombin, al the effect of thrombin on fibrinogen wa rather favorable. The anterior lobe extra defers all phases of coagulation as does als cholin.

According to Ischikawa and Sasaki th coagulation time in rabbits gradually increases with the feeding of thyroid gland, likewise the fibrinogen content of the plasma. Cantarow Cauen and Gordon report on an investigatio with subcutaneous administration of Collip parathyroid hormone in healthy persons They found — by no means constantly demon strable — a transitory increase of seru calcium, a slow rising of the blood calcium and an acceleration of the blood coagulatio Wohlgemuth and Hiruma found that afte ligature of the pancreas duct the fibrinoge content of the blood rises 2 to 8 times th normal value, while the thrombin conte of the serum remains unchanged. Paralle with the increase of fibrinogen there occurs a retardation of the coagulation process. L Barre shows that impure insulin preparation with regard to their cholin content, inhib the change of proserozyme to serozyme a well as the reaction of the serozyme with th

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serozyme. Pure insulin should not disclose this effect.

Concerning the Appearance of Sugar in the Urine with Insulin Injections. — Ernst Wichmann. (*Deut. Arch. klin. Med.*, 164 : 172, 1929.)

In a patient with icterus in whom there was demonstrable, at the height of the icterus, a diabetes among other disturbances of the carbohydrate metabolism of the liver, up to 17.6 gm. sugar per day were excreted in the urine after injections of insulin. The blood sugar was maintained at the lowest normal limit. After abatement of the icterus despite continuous insulin dosage, no more sugar was excreted into the urine. The author maintains that it is possible that in icteric patients, the insulin induces an electrolyte displacement in the blood or an altered formation of sugar in the blood. At any rate, with the administration of insulin in the treatment of non-diabetic patients, the appearance of sugar in the urine is henceforth to be expected.

Concerning the Antagonistic Relationship between Posterior Pituitary Hormone and Insulin. — Karl Velhagen. (*Arch. exp. Path. u. Pharmakol.*, **142** : 127, 1929.)

The investigation conducted by the author offers adverse testimony for the fact that insulin is an antagonist of the uterus-exciting and blood pressure-increasing hormone of the posterior lobe of the pituitary.

The blood sugar-increasing and insulin-antagonistic substance of the posterior lobe is contained in the pars neuralis as well as the pars intermedia. In order to inhibit the insulin hypoglycemia very large quantities of substance from the posterior lobe must be administered. Likewise, by means of repeated dosage of extract of the posterior lobe the action of insulin originating in the body is not suppressed. No diabetes mellitus occurs. Pituitary glycosuria can not be derived from increased dosage of posterior lobe secretion and therewith the particular inhibition of insulin action can not be increased. The secondary hypoglycemia which is often to be observed after administration of posterior lobe substance is probably the result of an enlarged insulin secretion. In animals with pancreatic diabetes the secondary hypoglycemia is lacking.

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Concerning the Action of Kidney Extracts on the Functional Status of Contracted Kidney. — Stejskal. (*Med. Klin.*, **25** : 983, 1929.)

A systematic organotherapy in diseases of the kidney by means of internal administration of kidney extracts was first instituted by Dieulafoy (1892).

The author obtained results with parenteral administration of kidney extracts in ten cases of primary and secondary kidney contraction which are of interest and have a general significance. The kidney extract was administered partly in the form of watery extracts and partly in such a form that the lipoid substance of the kidney was contained in non-autolysated form. This was administered to the patient in the form of an intracutaneous blister in amount from 2 to 5 cc., in order to insure slow resorption of the extract. The fact was brought out that, excluding any disturbing general reaction of the organism, the method of treatment was capable of suppressing the increased blood pressure of hypertonia which occurs in kidney diseases (primary and secondary kidney contraction). The influences on the blood pressure are organ-specific, *i. e.*, they occur only after injection of kidney extract and only in nephritic hypertonia. Decrease of polyuria was observed four times. The decrease of blood pressure in contracted kidney will also serve as a valuable therapeutic indication. Whether there is a relationship between the substance in kidney extract and the circulation hormone found in the urine by Frey, can not yet be stated. The most important fact of this contribution is the information that lipoid extracts of kidney also act on the blood pressure in contraction of the kidney.

New Therapeutic Investigations on Hydrops Articulorum Intermittens. — Hermann Schlesinger. (*Wien. klin. Wochenschr.*, **42** : 832, 1929.)

Up to the present time only a few more than a hundred cases of this disease have been known, of which number the author was able to observe fifteen (in 25 years). Only two of the patients were males. The cyclic course of the joint swellings was quite regularly interrupted by pregnancy. The author assumes a hormone dependence which is evident as a functional anomaly of the ovary. During pregnancy part of the function of the ovary is consigned to the placenta and the effect of the hormone produced by this agency is a much stronger one than that of the ovary. Following upon the improved function or the increased function, the swellings cease. The accuracy of this hypothetical explanation is supported by the therapeutic effect which was obtained by means of subcutaneous injection of placenta extract.

How Does One Treat Nervous Congestion and Sweating? — Spiegel. (*Mitt. Volksgesundheits.*, No. 6, 194, 1929.)

Besides a general quieting effect, an influence by means of ovarian and testicular preparations may be expected for disturbances of internal secretion (hyperthyroidism, hypofunction of the genitals) and a suitable therapy is to be obtained.

Concerning the Influence of Thyroid Gland Activity on the Depression of Red Blood Corpuscles. — E. P. Tschernosatonskaya. (*Zeitschr. ges. exp. Med.*, 66: 67, 1929.)

The speed of depression of blood corpuscles was studied in normal and thyreoprivic animals.

After thyroidectomy the reaction slows down so that the maximum retardation occurs 4 to 6 weeks after the operation.

After feeding of thyroid gland, depending upon the dosage, there occurs an acceleration of depression speed, of pulse, and an augmentation of lymphocytosis.

Lugol's solution in small doses has the same effect, but in slighter degree. The changes in depression speed can perhaps serve as an evaluation method for thyroid preparations.

The Influence of the Male Sex Hormone on the Female Organs of Generation and on Gestation Processes. Hormonal Sterilization and Interruption of Pregnancy in Female Animals. — Woldemar Reiprich. (*Arch. Gynäkol.*, 136: 417, 1929.)

The incretory influence of male sex hormone on the generation processes and generative glands was studied by means of twenty-five transplantations of testicle on female rabbits. It was possible to obtain by transplantation of fresh testicle tissue, hormone sterilization as well as interruption of pregnancy in female animals. The smallest effec-

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...ive amount (in rabbits) was about one-half ...a mature testicle, a positive effect was only ...to be obtained in the first half of pregnancy. In the case of successful pregnancy, a striking decrease in the number of offspring occurred with insufficient hormonal activity of the male sex hormone administered with the sex glands. The pathological-anatomical findings were: striking atrophy of the internal female genitals. In the gravid woman hormonal interception is not possible up to the present time. The investigation forms further positive proof for the laws of antagonism of the gonads.

On the Question of Endocrine Arthritis (Eunuchoidism and Morbus Bechterewi). — Jakob Ratner. (*Mitt. Grenzgeb. Med. u. Chir.*, **41** : 402, 1929.)

In a patient with typical eunuchoidism there existed spondylarthritis ankylopoietica. The question of whether it was an endocrine arthritis depends upon whether one can speak of an endocrine disease, if endocrine therapy serves good stead. In this sense one can speak of an endocrine arthritis. Although J. Bauer cautions against too great optimism with regard to endocrine therapy, he unjustly restricts the limits of this therapy. In order to know what this therapy is actually able to accomplish we must take every advantage of it and deliberate upon it profoundly.

Organ Extracts and Their Effect on Immuno-Biological Processes. — Pockels. (*Med. Klin.*, **25** : 975, 1929.)

Spleen and lung extracts were given *per os* to human beings to maintain the active di-immunization. A specific influence was derived.

Concerning the Effect of Parathyroid Extract on the Formation of Blood. — Stephan Pelláthy and Josef von Fernbach. (*Endokrinologie*, **3** : 406, 1929.)

The authors have investigated the effect of the Collip extract Parathormone on the formation of blood in various patients. The investigations show that the Parathormone exercises a positive effect on the formation of blood and that the effect evidently may be considered as hormonal, not as calcium activity, since it still remains when the calcium content of the blood is not raised, or in other words, since the changes observed are different from those described by other authors after administration of calcium. The red blood cell count suffered no significant change. The test was performed to count the white blood cells in five asthmatics, seven Basedow patients and in fourteen other patients after injection of Parathormone.

It was shown that with the administration of Parathormone an increase in count of myeloid cells occurs similar to that after adrenalin and thyroidin. There are similar changes in formation of the blood after stimulation of the sympathicus, when a leucocytosis exists. In as much as the sympathetic and parasympathetic formation of blood may be contrasted with each other, the action of parathyroid extract may be indicated as sympathicotonic; hence it can also be of value in that favorable results are to be obtained when it is administered in vagotonic diseases, in asthma, urticaria and serum sickness.

How May the Favorable Effect of Liver Therapy Be Explained? — J. Pal. (*Mitt. Volksgesundheits.*, No. 6, 194, 1929.)

Liver contains substances from the realm of the amines, which promote the formation of erythrocytes in the bone marrow, provided the bone marrow may be influenced. All kinds of liver which have been investigated up to the present have proved to be effective in suitable amounts, for example, even fish liver. On the quantitative basis calf liver, pig liver and ox liver are just as appropriate as bird liver. Fatty liver is not to be recommended since the same weight contains much less active substance. The administration of extracts simplifies the treatment.

Concerning the Effect of Spleen Extract on the Formation of Red Blood, Particularly in Hyperglobulia Vera. — Nipperdey. (*Deut. med. Wochenschr.*, **55**: 1085, 1929.)

The experiments of the author show that the extract form of spleen therapy, as far as concerns dosage and compatibility over a long period, is apparently simple, that to a great extent the subjective improvement was very much pronounced in all patients, in whom there occurred a considerable increase in weight. The dosage varied individually. With too small doses extensive objective harm may be caused by a polycythemia. This

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result shows that, according to the severity of the disease, the length of time it has existed and the age of the patient, the results of spleen therapy must be various. According to the reports given, up to the present, the therapy is exhausted, not in the transitory result of short periodic administration, but with proper dosage, without calling forth any harmful effects, it appears to have a better effect if administered longer.

The Effect of Liver Extract on the Disturbance of Diuresis in Kidney Insufficiency. — Hans Molitor and S. Glaubach. (*Wien. klin. Wochenschr.*, **42** : 889, 1929.)

From the cortex of the liver, by means of fractionated extraction according to a certain process, various liver preparations could be obtained which partly caused a diuresis-inhibiting, partly diuresis-promoting effect. It was shown in dogs with decrease of kidney parenchyma to one-quarter efficiency, that the water metabolism, after subcutaneous injection of 10 to 20 mg. of the liver extract, was almost without exception altered so that there was an increase in amount of excreted urine toward normal values and therewith an improvement in the general condition. The liver preparation acts in amounts of from 1 to 2 mg. per kg. of animal, it is water-soluble, has only a weak albumin content, is free from lipoids, bile acids and purin derivatives.

The Administration of Insulin in Oily Suspension. — O. Leyton. (*Bull. et mém. Soc. méd. hôp. Paris*, **45** : 779, 1929.)

The subject of the author is the administration of insulin in oily suspension. After numerous investigations with other oils, castor oil was found to be the most suitable. This oil can carry 100 units of suspended insulin per cc. Owing to its low degree of viscosity the oil must be heated slightly before the injection. The needle used for the injection can not be so fine as that used for watery solutions. The most important fact is that the injection be given not intramuscularly, but subcutaneously. It has been observed that these are the least painful. It is given in the morning before the patient rises. The author is satisfied with the results obtained with this method and he believes that other hormones may be applied with advantage in the same manner.

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Pharmacology with Reference to the Intestine. — Hans Molitor. (*Wien. klin. Wochenschr.*, **42** : 839, 1929.)

Adrenalin, the stimulating medium of the sympathetic, has hardly any value in administration to quiet the intestine; however, it is noteworthy that it could be observed in human beings, that each state of excitation, which evidently leads to an increased endogenous adrenalin production, is followed by a protraction of intestinal movement. The secretion of intestinal juice is regulated (at least in part) by a hormone, that is by means of secretin which is chiefly formed in the pars pylorica, and is released from this place into the blood stream to the intestinal glands in the fundus.

Leading Theories on the Treatment of So-Called Pyloric Spasm. — H. Mettenheim. (*Med. Welt*, **3** : 887, 1929.)

The existing disturbance of equilibrium of the vegetative nervous system can be based upon a weakness of the sympathetic; thus Paul (Frankfurter Children's Clinic) recommends injecting intracutaneously 4 to 5 times daily, shortly before meals, from 1 to 2 parts of a 1:1000 adrenalin solution. The effect lasts about 40 minutes. This therapy has been confirmed by the author as well as by other reporters (Finkelstein).

In the Treatment of Hyperemesis Gravidarum Can Insulin Be Substituted by Synthalin? — Köhler. (*Mitt. Volksgesundheits.*, No. 7, 227, 1929.)

A substitute for insulin in the treatment of hyperemesis does not seem to be entirely recommendable. Synthalin is not to be regarded as an absolutely harmless medium for there have already been several cases of injury to the liver after use of this substance. Since hyperemesis as well as other toxicoses of pregnancy are quite commonly associated with injury to the liver, synthalin medication would act as an additional injurious agent, which must be avoided.

The Treatment of Diseases of the Liver with Insulin and Grape Sugar with Regard to Young Children. — Knake. (*Zeitschr. Kinderheilk.*, **47** : No. 5, 1929.)

Simultaneous administration of insulin and grape sugar was used in severe symptoms of liver insufficiency and in slight cases of parenchymatous disease of the liver, for the purpose of maintaining or increasing the function of the liver for the final glycogen stage. Favorable results were obtained in the case of an 8 year old syphilitic girl, very icteric, with signs of severe liver damage which were to be accounted as acute yellow atrophy of the liver.

The Natural Immunity of the Child and the Possibility of Influencing It. — H. Kleinschmidt. (*Jahreskurse ärztl. Fortb.*, **20** : 17, 1929.)

Under the investigations for artificially increasing the natural immunity experiments with organ extracts are also to be mentioned. Recently interest has been directed to spleen extracts. The experimental foundations are at any rate very far-reaching. By means of prophylactically and therapeutically administered injections, Schröder was able to obtain a rise in resistance in tuberculosis-infected guinea pigs. In primary vaccination of guinea pigs Schlack found a definitely stronger, more lasting, and in secondary vaccination, a definitely weaker, more abrupt reaction than was exhibited by the controls. Thus an increased prophylaxis and hence also a stronger immunity was obtained by means of spleen extract.

Clinical and Experimental Observations on the Ovarian Hormone Folliculin. — S. Joseph and I. Raschkes. (*Deut. med. Wochenschr.*, **55** : 1044, 1929.)

Amenorrhea due to subfunctioning of the ovaries was improved in a portion of the cases by folliculin injections over a long period. Folliculin has the best effect in young operatively castrated individuals, in whom the therapy is commenced as soon as possible after castration. The choice of female patients is important for the success of the therapy, particularly in cases where associated diseases of other glands are to be expected. Intramuscular injection is as effective as intravenous.

The Action of Extracts of Endocrine Glands and of the Cardiovascular System of Warm-Blooded Animals on the Heart of Warm-Blooded Animals, *in Situ*. — G. J. Katz and E. A. Liebenson. (*Paris méd.*, **19** : 590, 1929.)

The authors worked with extracts of the following (14) organs: Right and left ven-

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tricles, heart auricles, vena pulmonis, aorta, lungs, bronchioles, liver, kidney, suprarenals, thyroid, testes, pancreas and spleen. The authors studied the effect on the heart *in situ* of a mixture of all of these extracts given by intravenous injection. For comparison, extracts of the ox, horse, dog and gull were derived. An experimental series was established with each one of these mixtures. The authors experimented with cats, dogs, rabbits and guinea pigs. In the investigations on cat hearts the authors found that the administration of the combined extract intensified the positive inotropic, and in the majority of the cases, also the positive chronotropic action of the heart. If the animals were previously chloroformed the combined extract strengthened the neuro-muscular system of the heart and made it more resistant. After preliminary nicotin injection the chronotropic action of the heart was first negative and then positive. Chlorammonium preceding the injection of the extract led to acceleration of the contraction and to its intensification. After previous treatment with morphine the contraction was likewise particularly strong.

A Clinical Method for the Assay of Insulin Preparations. — Karl Csepai and Bela Förstner. (*Endokrinologie*, **3** : 412, 1929.)

The method is based on the idea that the persistence of sensibility to insulin in one and the same person can be assayed so that it may be possible to control various insulin preparations as well as to estimate the sensitivity of a person to various insulin preparations. The effect of a freshly prepared solution of international insulin in the proportion of 1/15 unit per 1 kg. of body weight was tested on a chosen individual and on the third day thereafter the same amount of the insulin to be tested was given. By means of comparative curves it was possible to obtain relatively exact information as to the content of specific substance of the preparation in question.

An Essential Aspect of the Problem of Medical Application of Insulin. The Question of Degree of Purification of the Insulin Preparation. — H. Chabanier, C. Lobo-Onell, M. Lebert and E. Lelu. (*Presse méd.*, **37** : 766, 1929.)

For the purpose of successful antidiabetic treatment the entire diabetic process must be influenced, *i. e.* the acetonuria, the glycosuria and the hyperglycemia. And then care must be exercised that these symptoms do not return again. This is quite possible with only slightly purified insulin, which permits the interception of the symptoms and, in itself, is not dangerous. The result is otherwise with intensely purified preparations. Only small doses, such as are required in slight cases, and here, too, it was not difficult to correct the symptoms, were well tolerated by the patients. In cases of medium severity and in intense cases, in which one is forced to increase the dosage, secondary effects often occur which are prompted by the increased dosage. The difficulty of treatment lies in the fact that on the one hand the dosage chosen must be large enough to be effective and secondly, secondary symptoms must be avoided. The fact arises that with systematic treatment of diabetes with insulin only certain symptoms retire while others, for example the glycosuria and the acetonuria, still remain. In this instance very little has been accomplished with insulin. The success of the therapy rests with the adequacy of the dosage.

Concerning a Case of Acne Rosacea Accompanied by Endocrine Disturbances. — Bory. (*Progrès méd.*, **57** : 1011, 1929.)

In a 42 year old female patient who had suffered from obstipation for a long time, had been dyspeptic for 6 months and for 13 years was afflicted with a pustular cutaneous eruption of the face and a facial erythrosis, there were present all indications of a Raynaud symptom complex (numbness in the finger, violet color of the nose). The patient only began to menstruate at the seventeenth year, and at 40 reached the menopause, hence there was evidence of ovarian disturbances. Besides local medication and attempts to alleviate the dyspeptic symptoms, the patient also received pluriglandular therapy, namely thyroid gland, ovarian and testicular substance. More will be reported later concerning the ensuing process.

Concerning Cases of Pernicious Anemia Which Appeared Refractory to Liver. — Léon Blum and C. van Caulaert. (*Progrès méd.*, **57** : 1055, 1929.)

Report on cases of pernicious anemia which were left absolutely uninfluenced after certain liver extracts, while they reacted favorably to calves' liver and also to other extracts. The

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necessity of strict control of the activity of liver extract is stressed.

Unusual Insulin Damages to the Circulation and the Effect of Them on Carbohydrate Metabolism. — Reinwein. (*Deut. med. Wochenschr.*, **55** : 951, 1929.)

From two case histories it was shown that in insulin treatment of diabetics with heart trouble the effect of insulin on water maintenance must not go unconsidered, if one does not wish to expose the patient to the danger of increasing or causing an insufficiency of circulation. If such does occur, then the activity of the insulin is greatly lessened and the carbohydrate tolerance will be made much worse by large insulin doses.

Remarks on the Influence of Liver Substances on the Formed Elements of the Blood. — N. Reinitz. (*Skandinav. Arch. Physiol.*, **56** : 1, 1929.)

By means of investigations on healthy rabbits the author tested the influence of liver substances on the formed elements of the blood. It is thus shown that by intravenous injections of liver extracts an intense thrombocytosis as well as a weak lymphocytosis may be induced. In two instances the polymorphonuclears also showed a slight increase. As opposed to this, the injections produced no changes in the erythrocytes of healthy animals. Watery as well as alcoholic liver extracts are active, the former perhaps more so than the latter. Under certain circumstances liver extract can exercise a strong toxic effect, since it very rapidly induces respiratory paralysis during continuous heart activity. In normal animals liver extract is without effect on the erythrocytes and on the hemoglobin content. The occurrence of thrombocytosis implies that the liver extract exerts a stimulating effect on the red marrow.

Effects of Acetylcholin on the Secretion of the Pancreas. — Maurice Villaret, L. Justin-Besançon and Roger Even. (*Paris méd.*, **19** : 501, 1929.)

Inspired by the investigations of Desgret and the later investigations of Launoy, the authors studied the action of subcutaneous and intravenous injections of acetylcholin on the pancreas secretion in dogs. They observed that this substance causes the secretion of a juice which acts upon egg albumin and hence contains a primarily active trypsin. By means of ligature of the duct of Wirsung (pancreatic duct) and following this by injection of acetylcholin, similar to the experiments made by Binet and Brocq with pilocarpin, the authors essayed to induce a hemorrhagic pancreatitis. Once out of four attempts they obtained a pancreatitis with hemorrhagia and fat necrosis.

Functional Test of Blood Circulation. — Usadel. (*Therap. Gegenw.*, **70** : 224, 1929.)

The author gave hypophysin intravenously before operations in order to determine its action on the circulation. In healthy individuals a typical curve was obtained and in these cases the operation proceeded without any disturbance; in cases with an atypical curve, disturbances in the form of cardiac weakness occurred after the operation.

Influence of Thyroid Gland and Pancreas on the Carbohydrate Metabolism of the Liver. — Rudolf Siegel. (*Klin. Wochenschr.*, **8** : 1069, 1929.)

The disturbance of metabolism in diabetes is wholly and entirely to be considered as a deficiency of insulin in the organism. Nevertheless, we see how by means of impaired function the disorders of the endocrine glands come about, which have different characteristics for each organ investigated. The distortion of correlation occurring mostly in diabetes affects the ratio, to be counterbalanced, with regard to utilization of carbohydrate in metabolism in the thyroid gland and insulin effects in the end-organ. Since in the liver this antagonism is particularly important vitally, the disturbance of metabolism of the liver in the diabetic organism appears in the above defined form.

The Hammar Experiments concerning the Human Thymus. — B. de Rudder. (*Med. Klin.*, **25** : 812, 1929.)

Hammar's material comprises forty-six hyperplastic, post-fetal thymuses. In thirty-four instances there is evidently disturbance of the internal secretions. The predominance of disturbances of internal secretions with hyperplastic thymus presses the conclusion that the hyperplasia is only a symptom of an endocrine disease. The variable in thymus parenchyma is the leucocyte content and the presence of Hassall bodies. Leucocyte depression results in hypofunction or symptoms in the sex glands or suprarenals. Leucocyte

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excitation results in hyperfunction of the thyroid, and apparently also of parathyroid and pituitary.

Dietetic Stimulation Therapy. Concerning the Modern Treatment with Endocrine Glands. — Wilhelm Schlesinger. (*Wien. med. Wochenschr.*, **79** : 772, 1929.)

The investigations on the administration of vitamin and hormone present the conclusion that both of these substances function as a simple equivalent for the substance lacking in the organism, to activate protoplasm. Hormones as well as vitamins are thermolabile and hence all glands are effective if they are taken raw or only slightly cooked. In cases of latent malaria, in which proliferation of the gametes with true malarial symptoms were evident, the author instituted experiments with thymus and effected a stimulation with *per os* administration. Müller and Del Campo found increase of muscle activity after injections of thymus extract, Bier recommends thymus feeding in healing torpid processes; the action of thymus on bone growth is generally well known (Hass and Glässner). Gudernatsch and Romeis observed increase in propagation when tadpoles were fed thymus substance. This can lead to the investigation of the administration of thymus in hypofunction of the female sex glands. Birkler administered spleen in large amounts in various dermatoses and found a predominantly favorable influence in cases of neurodermatitis, and likewise in allergic conditions of the skin with definite eosinophilia. The results of administration of spleen in cases of tuberculosis are to be considered in the light of a stimulation therapy. The results of spleen therapy in tuberculosis of the bones accords with the finding of Meyer that after involution of the thymus the spleen takes up the function of the thymus. Liver which plays such an important part in the treatment of pernicious anemia, is extremely rich in ferments. Such ferments consist of, besides other factors, the power of forming amino acids, and thus the liver may be considered to be in direct co-operation in the formation of albumin and therewith the prevention of the formation of toxins in the blood, because of its ferment content. It is noteworthy that all authors are agreed that liver, as such, acts better than liver extract, and above all, the administration of heat must be moderate. Hence the active substances are thermolabile and this is consistent with the assumption that the liver ferment is the active agent.

The Action of Several Medicinal Preparations on the Function of the Stomach with Considerations of Blood Pressure, Pulse and Blood Formation. — Ernst Schwab. (*Zeitschr. ges. exp. Med.*, **65** : 782, 1929.)

The author conducted experiments on twenty-two patients to determine the effect on the function of the stomach of 0.01 mg. Suprarenin hydrochlor. synthet. Höchst.

In fifteen patients with no organic gastric disorder there was found six times reduction and five times increase of the acid values; in three cases there was no variation found in the trend of the curve. In five cases of Ulcus duodeni there always occurred decrease in the acid values. In one case of periduodenal adhesions and in a case of Ulcus ventriculi there was a significant increase of acidity. In nine instances without organic gastric disorder the time of evacuation was increased by the administration of adrenalin, in three instances it was unchanged; in three cases of Ulcus duodeni it was deferred and twice it was increased. Influence of the amounts of secretion, of post secretion and of the duodenal reflux were not definitely determined. There was an increase in systolic blood pressure. The pulse was increased in three cases. The blood picture showed a definite increase in leucocytes. In general, nothing can be said for conclusive results as a functional test.

Relationship between Diseases of the Blood and Diseases of the Digestive Apparatus. — Emil Schwarz. (*Wien. med. Wochenschr.*, **79** : 738, 1929.)

The results of liver therapy in pernicious anemia are an indication that the toxic action as well as the so-called hemolytic process in pernicious anemia can be successful otherwise than has been assumed. The author does not agree with the broadened opinion of the day, that liver therapy is a simple symptomatic method, a stimulant for the bone marrow, and he assumes further that the liver has a specific rôle in the formation of the blood. Hence it is shown that the megaloblastic formation of blood in the embryo is released at the instant the normoblastic is released if the liver cells are differentiated from the primordial cells of the embryo and further that no

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after remission of pernicious anemia like that of liver feeding, permits the return to normoblastic, orthochromatic type.

Concerning the Action of Kidney Extracts on a Functional Basis in Contracted Kidney. — K. Steyskal. (*Wien. klin. Wochenschr.*, **42** : 696, 1929.)

In seven cases of part primary, part secondary kidney contraction, it could be shown that by means of intracutaneous injection the hypertonia of the kidney could be abated. In cases of non-nephritic hypertonia, kidney extract failed to act. Hence, it is a matter of specific organ effect of tissue extracts, which could likewise be called forth with lipoid extracts of the kidney.

The Whipple Cure and the Modern Treatment of Pernicious Anemia. — Paul Véran. (*Rev. méd.*, **46** : 325, 1929.)

Patients with pernicious anemia are not treated the same way in France as they are in America; other methods are used more often, such as blood transfusion and insulin therapy. The result is that the statistical data concerning liver therapy do not present the clear picture they do in America, where this treatment is given exclusively.

It is impossible to indicate either generally or specially the necessary duration of liver therapy. Recurrence of the disease or relapse due to intercurrent disease occurs occasionally, but these cases are always actively combated with the newer liver therapy. E. Bernard and Deslenquois, in a case of pernicious anemia due to bronchitis, have observed a diminution of red blood cells from 3.6 millions to 2.2 millions and a very abrupt rise of the erythrocytes occurred after liver therapy. Daily ingestion of liver has to be reinstituted each time the symptom reappears in the patient treated, hence liver extract will be of good service for the intermittent medication. After too lengthy use of excessive dosage, aggravation of the disease symptoms was observed. In a patient with kidney disease, who was undergoing liver treatment without the control of a physician, anemia occurred. Pal observed the occurrence of high arterial blood pressure in a patient who became erythremic. Hence consideration must be given to the problem of large doses of liver throughout a long period of time, lest adverse results ensue.

The practical significance of liver extract is great, nevertheless there is no adequate proof as yet, whether there is a definite advantage in the effect of liver extract.

Concerning the Advancement of Bone Growth by Means of Injections of Bone Extract. — Carla Zawisch-Ossensitz. (*Wien. klin. Wochenschr.*, **42** : 733, 1929.)

Comprehensive researches of the author give the following results:

In the bones of young animals, in particular those of animals in the period of greatest growth, there is present a ferment, which is in apposition with organic bone substance or promotes it and which is differentiated from the calcium phosphate designated (Robinson) hexosemonophosphate. The author was concerned with obtaining it in pure state.

By means of the injection of a bone extract containing the ferment, an improvement may be derived in the growth of bones of young animals. The action is not one of a stimulant, but is specific and could be initiated in animals of the same species as well as those of another.

Moreover, its administration causes no unpleasant secondary effects and since the extract is much more applicable locally than generally, there is nothing to hinder osteotherapeutic tests on human beings.

Estrous Hormone in the Bile. — M. A. Gsell-Busse. (*Arch. exp. Path. u. Pharmakol.*, **139** : 328, 1929.)

The author demonstrated that Na-taurocholate contains an active principle which acts in the manner of an ovarian hormone. Further investigations show that the action is not inherent in the acid taurocholate or in the acid bile salts. The estrus-producing action does not originate with the cholate either, but from a combination of cholates. The active substance is insoluble in pure water, but soluble in most lipoid mediums. Of the animal biles, ox bile is the best speculation. Hog and dog bile exhibit the lowest value of activity. Allen and Biedl found that there is no estrous hormone to be obtained from the placenta of hogs and dogs. In seventeen experiments with human bile, coming from women, all were active. Fourteen experiments on bile from men proved apparently less active than that from women. Further experiments were conducted with liver extracts from animals. It was found that the total lipoid extract of 0.5 kg. of fresh

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liver was not entirely inactive, that is, that 0.5 kg. of fresh liver did not contain 1 rat unit. In two instances of pregnancy no estrus-inducing substance was demonstrated. Meconium contains the greatest promise up to the present (1 kg. calculated to contain 6000 rat units). The author holds the opinion that the placenta as the place of origin of the estrus-inducing substance is not definitely determined and he considers the possibility that the embryo bile, that is the embryo liver, during pregnancy is the site of production of the estrus-inducing hormone.

Concerning a Hormone of Heart Motion. II. Contribution. Further Experimental Investigations with the Heart Hormone Preparation. — L. Haberlandt. (*Pflügers Arch. ges. Physiol.*, **221** : 576, 1929.)

In new tests with the heart hormone preparation which has recently been obtained histamin-free the pulse-inciting, pulse-accelerating and pulse-strengthening activities of the heart substance were demonstrated on isolated frog ventricles, using dilutions of 1:10 million; also the rhythmic and positive dromotropic effect observed in earlier experiments, in general were observed in frog hearts which had been isolated two days previous.

By means of suitable doses of the preparation the sensitivity of the frog heart chamber was increased so that with further dilution definite action of the heart was obtained. Such a sensitization could also be obtained with treatment of the animal for several days in the form of injections into the lumbar lymph sac.

Strong concentrations of heart hormone preparation, for example 1:100, can, under certain circumstances, but must not cause an inhibiting action.

The heart hormone preparation decreases the tendency of the frog ventricle to deteriorate with faradic stimulation of the atrioventricular region in surviving network.

Pharmacological Researches on the Heart Hormone Preparation. — L. Haberlandt. (*Med. Klin.*, **25** : 329, 1929.)

The investigations of the author have shown that the action of digitalis substance on frog hearts previously treated with heart hormone preparation, in the most cases, was increased, in contrast to the control hearts. In this instance the sensitizing effect of the heart hormone preparation was shown to be strongest with strophanthin, weaker with digipuratum, and weakest with squill. The clinical importance of sensitivity to digitalis substance obtained by means of heart hormone treatment is close at hand. Further it was demonstrated in another series of experiments that the capacity for resistance of the isolated frog heart against chloroform and ether narcoses after previous treatment with heart hormone preparation is, in general, greater, and its capacity to relax is increased. This rise in resistance to organ narcosis which has been demonstrated by means of the heart hormone preparation, will also be valuable in general narcosis, hence its practical value.

The Laurence-Biedl Symptom Complex. — Hertzog. (*Zeitschr. Augenheilk.*, 67 : 176, 1929.)

In two brothers suffering from obesity, dystrophia adiposogenitalis, polydactylism, disturbance of mental development and retinitis pigmentosa thyroid therapy was instituted with the result that in one patient the acuteness of vision was somewhat, and in the other very much improved.

Communications on the Initiation of Birth According to Stein. — Max Widers. (*Zentr. Gynäkol.*, **53** : 403, 1929.)

The process according to Stein, for initiating the birth process at the termination of pregnancy is as follows: In the morning early, two teaspoons of castor oil, 2 hours later 2 drops of pituitrin, and then twice every hour two drops of pituitrin were given. If at this point the labor pains began the pituitrin doses were resumed intramuscularly several times, with the result that the birth process was ended by evening. In failure to succeed the medication was instituted again on the second and third days and 60 to 70 per cent of the women reacted, *i. e.* if the uterus was actually capable of producing labor pains. The period of pregnancy must have reached its termination. This is a prerequisite. The reports on the matter are variable. Hatzky (Hamburg) reports 30 per cent success, v. Kries reports no success, Adler (Münich) 61 per cent and Eversmann 100 per cent. The author conducted the experiment on forty-four women during the past year with 75 per cent success. The indications for medical intervention in the birth process at the ter-

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mination of pregnancy are: 1. A medical indication, infection. 2. A social indication, shortening of the duration of the process. The advantages of the method are: 1. Total harmlessness for the mother. 2. Decrease in the length of the labor process. 3. The process is also entirely harmless for the child. 4. The afterbirth and hemorrhage after parturition have never been observed by the author.

On the other hand it is emphasized that medical intervention in the birth process is suitable only to be carried on in the clinic, and not in the practice, for one can not give to a midwife such variable remedies as the pituitary preparations. Under the accurate control of a physician, however, the Stein process is entirely without harm to either mother or child. The necessity for giving many injections is to be noted as an unpleasant circumstance, for many women have an aversion to the needle.

Diabetes and Pregnancy, Particularly concerning the Hormonal Relationship between Mother and Child. — Ernst Holzbach. (*Zentr. Gynäkol.*, **53** : 641, 1929.)

Casuistic contribution: A female diabetic who had cohabited for a long time and only first conceived after she had been treated with insulin and was sugar-free. Henceforth, one may be sure that more than the present 5 per cent of diabetic women will become pregnant if a greater number are treated with insulin. Many women are rendered entirely amenorrheic by diabetes, whereas in others after monthly amenorrhea menstruation is again instituted only after long treatment with insulin. The patients observed by the author were as good as sugar-free until the termination of pregnancy. Pregnancy also had a happy outcome in cases of disorders of metabolism. On the first day after parturition there again occurred a pronounced hyperglycemia in the mother.

Continued Investigations concerning the Influence of Insulin on the Respiratory Metabolism. — Cai Holten. (*Biblioteek for Laeger*, **121** : 49, 1929.)

The respiratory quotient rises in normal individuals after the injection of insulin, doubly as high as in diabetics. Concerning blood sugar the result is contrary, and the blood sugar is greater in diabetics than in normal individuals. Heat production increases in normal individuals after injection of insulin exactly as it does in those who have not received insulin. In normal persons insulin effects no changes in heat production, whereas it appears to cause a decrease in production of heat.

Parallel with the rise of CO_2 and heat production in normal individuals, the amount of ventilation increases about 16 per cent.

The respiratory quotient of diabetics after 12 to 14 hours following insulin injection is evidently higher than the existing process of oxidation accords and it is on the basis of formation of fat from carbohydrate. This synthesis ceases after administration of insulin. The drop in energy requirement which insulin seems to cause in diabetics is directly connected with the synthesis, since in this way a loss of energy is effected.

Genital Hemorrhages in Young Girls. — Kermauner. (*Wien. klin. Wochenschr.*, **42** : 297, 1929.)

Of the remedies for stopping hemorrhages, Kermauner prefers to give pituitary preparations besides the old medicaments. In pronounced hypoplasia ovarian preparations are also to be given, but only the best and most effective, and these only for a short time, so as to avoid an eventual too strong reaction.

On the Action of Several Amines. — H. W. Knipping and J. Steiger. (*Zeitschr. ges. exp. Med.*, **64** : 594, 1929.)

Several substances, such as adrenalin, acetylcholin, histamin, thyroxin, atropin, pilocarpin and others, were tested in general with regard to their effect on energy maintenance. The experimental animals were rats, rabbits and dogs. The chemical substances mentioned are related to one another in their identity with the group of amines. Thyroxin and histamin appeared particularly active, and also adrenalin with limitations. The action of adrenalin given *per os* fails, and in the case of thyroxin is very uncertain. In the case of thyroxin, besides a slight demonstrable action with other dosage, there occurs a specific cumulative action, which is not to be seen in other substances. Daily administration of thyroid gland combined with 0.0001 gm. organic iodin for a month produced a strong rise in metabolism, culminating in a maximum in a few weeks.

Increase of oxidation by means of adrenalin is not so great as one would expect from the

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general findings, while the rise of almost the whole process is dependent upon great muscular unrest. In contrast to the other total oxidizing, energy-increasing substances, in the adrenalin test, no relief from sleep was to be derived.

With coincident administration of adrenalin and histamin, instead of the expected rise in metabolic activity, there was found a great intensification with greater unrest of the animal. It is noteworthy that the secondary action of increased basal metabolism is much greater than with histamin and adrenalin alone.

Acetylcholin in suitable dilution arouses the parasympathetic nerves and the organs innervated by them. In the author's experiments the effect of 2 mg. acetylcholin chloride was slight. The action of thyroxin is basically different from that of other substances in that in acute tests it is slight, and in contrast, with longer administration, a sluggish action occurs. At best the metabolism can in general be increased by means of increased thyroidin dosage in 40 per cent of normal individuals, without incurring any noteworthy secondary effect. The same holds true in thyroxin experiments. The activity of thyroxin which is less when administered orally than when given parenterally is certainly to be traced to a destruction in the intestinal canal and is important practically if one considers that with natural thyroid gland substance given *per os* the same effects are obtainable with parenteral administration as with oral. Hence one would be bound to thyroxin injection.

Studies on the Physiology of Hunger Activity in the Digestive Apparatus. I. Contribution. Concerning the Kind of Hunger Movements of the Digestive Apparatus in Experimental Hyperthyrosis.

With persistent feeding of thyroid gland there was observed: 1. A permanent increase of hyperthyroid disturbances in the hunger movements of the intestine, which is apparently dependent upon a functional accumulation of thyroxin. 2. After 1 month feeding with thyroid gland — a continuous after-effect (in the course of 10 months) which induced an intermittent reappearance of typical hyperthyroid disturbances of the peristaltic action in hunger. 3. The two-fold character of the peristaltic action of the intestine of the dog in hyperthyrosis — namely excitation and depression — rests upon various functional adjustments of the parasympathetic section of the vegetative nervous system in the digestive apparatus. 4. The effect of thyroxin on the activity of the digestive apparatus during hunger in experimental hyperthyrosis permits the assumption that the functional condition of the thyroid gland plays an essential role in the mechanism of peristaltic action in the digestive apparatus during hunger.

Studies on the Physiology of Hunger Activity in the Digestive Apparatus. III. Contribution. Concerning the Influence of Cholin on the Hunger Movements of the Intestine. — Alexander Kratinoff. (*Zeitschr. ges. exp. Med.*, 64 : 404, 1929.)

The effect of cholin on the hunger movements of the intestine of the dog was studied. With intravenous injection during hunger it was shown that cholin exercises a periodic contraction of the already instituted movements; in subsequent movements cholin increases the amplitude and raises the tonus. The subsequent contractions of the intestine as isolated and denervated by Heidenhain were greatly increased by means of cholin. In agreement with the data of Le Heux and other authors, and on the basis of experiments conducted by himself, this author considers the premise to be quite correct, that cholin is to be regarded as a hormone of peristaltic action of the intestine.

Concerning the Daily Fluctuation of Adrenalin Effect in Human Beings. — Martha Lanwer-deHaan. (*Zeitschr. ges. exp. Med.*, 64 : 534, 1929.)

In healthy and diseased persons there was found a significant daily fluctuation of the reactivity to subcutaneously administered adrenalin. The adrenalin injection entered more rapidly in the afternoon than in the morning; the eruption was in general stronger in the morning hours than in the afternoon or evening. The lowest place of appearance seemed favored by the relatively stronger reaction. By means of this daily variation which was also observed in pulse, blood pressure, leucocyte count, infiltration and general reaction, the sensitivity of human beings for adrenalin is differentiated from sensitivity to all other chemical substances up to the present time.

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Concerning Hypertrophy in Pregnancy. —Hermann Knaus. (*Münch. med. Wochenschr.*, **76** : 404, 1929.)

On the basis of clinical investigations Halban presents the opinion that there must be, above all a hormone or a ferment of the placenta which limits the hypertrophy of the musculature of the uterus in pregnancy.

On the basis of biological investigations the author comes to the conclusion that the corpus luteum acts to further the development of the mucous membrane of the uterus while the function of the endometrium has an inhibiting effect, and indeed is influenced by the interrupted activity of the pituitary extract. On the other hand the placenta provides hormonally for the hypertrophy of the uterine musculature.

What Medical Therapy Is to Be Instituted in Cases of Melancholic Depression. — Kogerer. (*Mitt. Volksgesundheits.*, No. 3, 99, 1929.)

Upon consideration of the doubtless ever-present participation of the vegetative and endocrine systems, in each case a hormone therapy is to be essayed, either with any one of the reliable thyroid gland preparations if there is no contraindication (vagotonic symptom) or, on the other hand an energetic sex gland treatment is indicated.

Diseases of the Central Nervous System and Digestive Tract. — Alexander Pilcz. (*Wien. med. Wochenschr.*, **79** : 267, 1929.)

Kogerer gave insulin injections in five cases of tabes with intestinal crises, for example, on the first day, 5, from the second day on, daily, until one day after the cessation of the symptoms, 8 clinical units subcutaneously; hypoglycemic shock was never observed. The usual desire for sugar ½ hour after the injection could always be satisfied. It was possible often to abort the symptoms and to lengthen the pain-free intervals. Kogerer rightly brought out the advantage of the harmlessness of this therapeutic method of insulin injections. In a series of investigations on thirty cases of tabes with pronounced painful symptoms, of whom twelve had gastric crises, Kogerer and Halpern determined the blood sugar content and found it more or less increased (105 to 135 mg. per cent) while in sixteen cases of tabes without notable sensible secretory stimulation symptoms, the blood sugar content hovered between 90 to 116 mg. per cent.

Bolten summarized Quincke's disease as well as colica mucosa (enteritis membranacea) and also epilepsy, asthma, etc., under the classification of exudative paroxysms and recommends the administration of hormone, namely preparations for accelerating the endocrine glands (thyroid glands, adrenalin).

Consideration of the Treatment of Anemia with Liver. — N. G. Lupu and R. Brauner. (*Bull. et mem. Soc. med. hop. Bucarest et Soc. sc. med. Cluj*, **11** : 4, 1929.)

Successive description of six cases of anemia of varied etiology, which were all treated with roast liver, with good results. Patients who could not tolerate liver in this form could take it prepared according to the American method, in puree form or as orangeade. If the treatment is intercepted the symptoms of anemia again appear. Good results can always be obtained with liver treatment if the bone marrow is capable of regeneration. In one case of malarial splenomegaly good results were obtained; in one case of malarial cirrhosis with anemia the therapy was without success.

Studies on the Action of the Female Sex Hormone in Parabiosis Experiment. — Mahnert. (*Krankheitsforschung*, **7** : 79, 1929.)

The author's investigations present the fact that the female sex hormone which circulates in the body of one animal passes over to the partner in the case of successful parabiotic union of two animals, for there is shown in the uterus and its sheath the direct effect characteristic of ovarian hormone. The hypothesis for the success of the method is based exclusively on the treatment of ovariectomized animals.

The Endocrine Glands and Methods of Rejuvenation. — P. Niehans. (*Schweiz. med. Wochenschr.*, **59** : 255, 1929.)

Each organotherapeutic method, that is, method of treatment with gland extracts, is based upon the assumption of the absence of zoological specificity of the hormone, *i. e.* on the implication that the glands concerned in human beings and those in animals have the same function, to secrete the same kind of substance and to produce the same hor-

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mone which is constant for each given gland. The internal secretion of the gland of an ape, of a dog, of a sheep, etc. is identical with the secretion of the corresponding gland in the human being. The results obtained with industrially prepared organ substances are often only slight and insignificant if they are not given throughout the life of the patient, often several times daily. How then shall we administer by oral route a desiccated, pulverized gland, obtained by incalculable chemical and other processes, whose content of active substance is in no way certain, if it is possible to transplant a fresh living gland with the temperature of the animal body, under aseptic precautions.

The author reported concerning his own successful transplantation of various glands in various disease conditions as well as in children and in old people. The mortality from operation is zero.

Concerning the Cachexia of Cancer and the Manner of Combating It. — Pal. (*Wien. klin. Wochenschr.*, **42** : 321, 1929.)

The struggle against cachexia is an important factor. Cachexia is perceived as a symptom of endocrine insufficiency to which is ascribed the interrelationship of various glands such as the suprarenal cortex, the spleen, the sex glands. Stephan derived an extract from the suprarenal cortex which he called "Nerihormon." This hormone stimulates the formation of erythrocytes when given by subcutaneous injection.

The author came to the following conclusions:

In the bone marrow of the cancer cachexia patient it is possible to cause a regeneration of red blood corpuscles by certain substances of a series of biological amines, and therewith to improve the condition of the patient. Of the injectible preparations of the present time Pal found that the suprarenal cortex extract is effective. Histamin, because of its toxic reaction in subcutaneous administration is not valuable. Considering the duration of treatment, substances which can be administered orally are most satisfactory. Concerning liver, there are data given in the literature which indicate that liver therapy had no effect on cachexia of cancer (Seyfarth and others). In several cases of anemic cachexia — and also in carcinoma — the author himself has observed recovery after liver therapy as well as after liver extract treatment. It is true that not every case reacts. The pa of recovery lies through the bone marrow.

On a Case of Tetany Due to Hypofunction of the Parathyroids. Good Results Obtained with Collip's Parathormone. — C. J. Parhon. (*Bull. et mém. Soc. méd. hôp. Bucarest et Soc. sc. méd. Cluj*, **11** : 1, 1929.)

A 40 year old woman suffered for 15 months with spastic symptoms which upon investigation proved to be manifestations of tetany. This was associated with great decrease of the calcium content of the blood. The patient received as treatment 20 units, subcutaneously, daily, of Collip's Parathormone. The tetany symptoms receded; a blood test showed hypercalcemia. With interruption of the injections the symptoms reappeared.

The Collip extract was prepared from the parathyroid glands of animals by means of hydrolysis with diluted acid salt solution. Collip, Liser and Schaphardson, Snelle and Habein have obtained good results in human beings.

The Regulation of Carbohydrate Metabolism. The Excretion of Insulin by the Kidneys and Related Parts. — Alexander Partos. (*Pflügers Arch. ges. Physiol.*, **221** : 562, 1929.)

The author obtained insulin from the urine with a slight modification of the Collip method. The extract contained besides the insulin, chiefly creatinin.

It was demonstrated that insulin is a normal constituent of human as well as rabbit urine. In fasting rabbits there is no insulin in the urine.

In a condition of hyperglycemia the urine excreted contains no insulin; as soon as the blood pressure begins to decrease, however, insulin appears in the urine.

In human as well as in experimental pancreatic diabetes no insulin can be demonstrated in the urine.

Continuation of Researches on the Heart Hormone. The Active Constituent of the Frog Heart Hormone of Haberlandt. — R. Rigler. (*Pflügers Arch. ges. Physiol.*, **221** : 509, 1929.)

The hormone, derived according to the latest contributions of Haberlandt, in this case was not the hormone of the frog heart, but the bull, and presented, not pure sub-

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stance, but rather an extract, with which excitation of the heart was possible also in warm blooded animals, as stated; in addition it should lower the blood pressure by dilatation of the blood vessels. According to the author's experiments the frog heart hormone of Haberlandt is endowed for its effect, with two different substances. The one alters the force and the other the rhythm of the beat. Reduction by burning to ashes brings out the inotropic but not the chronotropic action of the frog heart hormone.

The chronotropically active constituent of the frog heart hormone is potassium, the inotropically active portion corresponds to the Clark substance.

Under the limitations of the author's experiments the potassium threshold of the frog heart represents a Ringer solution with 165 mg. KCl per liter.

The Extraction of the Female Sex Hormone and Information concerning Folliculin Therapy. — Serdukoff. (*Gynécol. et Obstét.*, **19** : 39, 1929.)

The follicle has the following significance for the female organism.

It acts 1, as a generative agent; 2, as a protection for the uterus; 3, as an influence on the periodicity of function of the female organism; 4, for sensitization of the mucous membrane of the uterus for implantation of ovum; 5, for strengthening the heart contraction (Beloff); 6, liquor folliculi has a hemostatic effect; 7, as an influence on the secondary sex characteristics and on bone growth; 8, as sympathicotropic influence; 9, for sensitization of the uterus muscle for contraction; 10, for regulatory increase of secretion of isolated parts of the sex glands. Folliculin therapy is of three kinds. 1, in the form of fresh liquor folliculi from the ovary of the hog, 2, as an oily solution, and 3, as a watery solution. Fresh liquor folliculi, in general, forms no coagula, not even after 24 to 36 hours. The oily solution is an emulsion in which there are amorphs after the contraction of the albumin of the folliculin. The watery, albuminous solution is slightly opalescent; it can be put up in ampoules, but loses some of its strength after long storage.

The author conducted folliculin treatment in 125 cases of women between the 14th and the 50th years, especially for headaches, vertigo, congestion, vomiting, migraine, general weakness, irritability and fatigue.

The therapy is applied in the following cases: In cases of atrophy of the uterus with hypo-ovarianism, in cases of congenital aplasia of the uterus, in post-operative atrophy of the uterus with obesity, in the menopause, in habitual abortion, in meno-metrorrhagias of puberty, in malposition of the uterus, in adiposogenital dystrophy and in acute inflammatory processes. The therapy was confined to folliculin administration in 75% of the cases, in 25% calcium was also injected intravenously.

The results were satisfactory with regard to objective findings as well as subjective. Blood tests 24 hours after the commencement of treatment also confirmed this. The lymphocyte count rose about 10 to 20 per cent, that of the eosinophils about 2 to 4 per cent; further a shift to the left (Schilling) was observed. Blood pressure showed an increase 2 to 3 hours after the folliculin injection. The blood calcium content remained unchanged. The secretion of the vagina showed an increase of epithelial cells and an alkaline reaction, which lasted about 24 hours. The general findings and the constitution of the patients were very much improved after 2 weeks of treatment.

The Utilization of Spleen Contraction by Means of Adrenalin in Spleen Operations. — P. E. Weil and R. Grécoire. (*Presse méd.*, **37** : 326, 1929.)

For the purpose of obtaining contractions of the spleen in spleen operations the authors injected adrenalin. The following results were thus obtained in three cases of primary splenomegaly: Once the spleen was rendered entirely bloodless, in the second case it contained only one-tenth of its former blood supply and in the third case the evacuating action was quite weak and gave no measurable result. Usually this organ contained one-fourth or one-fifth more blood than its own weight.

The injection of 1 mg. of adrenalin should be made $\frac{1}{4}$ hour before splenectomy. It is possible to predetermine to a certain degree the effect of the adrenalin injection in a special case if, on the day preceding the operation a test injection is made and the change in spleen volume obtained by means of diagrams. The adrenalin injection spares the patient the loss of a large quantity of blood; in itself it is harmless and lessens the severity of the secondary consequences.

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Action of Hormotone Curative, Not Palliative

The therapeutic effect of Hormotone in dysmenorrhea is that of restoring a disturbed endocrine menstrual mechanism to normal. It is not a palliative effect. The results obtained at the Woman's Hospital, Soho Square, represent a cross-section of the experience in general medicine.

"Fifty cases were treated by organotherapy . . . . The majority were treated with Hormotone as follows . . . 46 of the cases so treated were relieved."



Dose: 1 to 2 tablets t. i. d. started preferably 2 to 3 weeks before the menstrual period.

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The Therapeutic Application of Acetylcholin. — M. Villaret and L. Justin-Besançon. (*Lancet*, **216** : 493, 1929.)

The vagal activity of acetylcholin, which has been determined by Henri Frederico, makes it clear that this substance is considered by several physiologists as a vagal hormone. Acetylcholin effects an excitation of the smooth musculature and in extraordinarily strong dilutions causes peristaltic activity in the isolated intestine. Acetylcholin is given either subcutaneously or intramuscularly; intravenous injections are dangerous, oral administration seems to have no effect. Besides its influence on the arterial blood pressure, its action on the heart, muscle and blood is noteworthy. It is given therapeutically on the basis of the fact that its vasodilatatory property is localized in the arteries and arterioles and that it possesses a similar influence on the vago-sympathetic system. The author, as well as others, gives acetylcholin in Raynaud's symptom complex, gangrene originally from arteritis and in similar disturbances. In diabetic arteritis the administration of acetylcholin plus insulin is more effective than insulin alone. Kalt contributes a very interesting case of thrombosis of the retinal artery with blindness which presented extensive improvement from the time of the first injection. The author has observed that the profuse sweats in tuberculosis patients are improved in a remarkably favorable way by means of treatment with acetylcholin.

Experimental Studies on the Functional Significance of the Theca Interna Cells. — Axel Westman. (*Acta obstet. et gynecol. scand.*, **8** : 290, 1929.)

The author conducted experiments on rabbits in order to test whether the cells of the theca interna have the capacity for producing hormone which is the analogue of that derived from the follicle cells. The experiments provide definite basis for the assumption that an apparently swift atrophy occurs in the cells of the theca interna when the follicle is divested of its granular membrane and thereby inhibited from forming corpus luteum. At any rate the results obtained indicate the fact that the theca cells in the wall of a mature follicle are not unable to produce the characteristic reaction of corpus luteum in the uterus, after the follicle has been deprived of its granular membrane. The author raises

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the question whether various hormones which effect a reaction in the vagina, such as changes in the mucous membrane, will be produced in the ovary.

Action of the Anterior Lobe of the Pituitary on the Development of the Genital Tract. — Watrin. (*Bull. soc. d'obstet. et de gynecol. de Paris*, No. 6, 433, 1929.)

The author investigated for 1½ years the possibilities of pituitary activity on guinea pigs not yet sexually mature. He comes to the conclusion that transplantation is a more reliable and scientific form of test than injection of pituitary extract and that the ensuing activity is more of a quantitative than of a qualitative nature. Further, the author believes that the changes in the uterus and in the vagina are definitely connected with the ovary.

Action of the Anterior Lobe of the Pituitary on the Ovary Treated with X-Rays. — A. Walter. (*Endokrinologie*, 4 : Part 1, 1929.)

Two months after x-ray therapy of the ovary with dosage considerably above that causing sterility, a total disappearance of follicles is obtained, then there is found on all sides, theca cells full of lutein. Such an ovary is able, however, to sustain the rut cycle, usually a permanent estrus follows. For the creation of estrus then an ovum or fresh corpus luteum is not necessary, but the theca cells must be the hormone agent or generator. When implanted with anterior lobe of the pituitary gland the ovary of very young mice which have been treated with x-ray only acts during the first week (provided not all the ova have been destroyed) in the manner similar to that of follicle maturity and the formation of corpus lutea atretica. Later, when the ovary consists only of lutein tissue, it reacts no more to implantation.

Concerning the Combined Action of Quinine and Pituitary Gland on the Puerperal Uterus of the Living Cat. — K. Schübel. (*Klin. Wochenschr.*, 8 : 1555, 1929.)

Quinine is a general cell toxin which arrests the anabolistic as well as the catabolistic processes in the cell. The point of attack must be sought for in the enzyme. The diversiform activity and applicability of quinine and its derivatives must be attributed to this influence of the cell. Of particular interest is the manner of the secreting and acting on the uterus. After per os administration at the most 3 per cent appears in the blood, after 24 hours the quinine is secreted. After intravenous and intramuscular injections two-thirds of the quinine is destroyed in the organism, the rest is retrieved after 8 hours. Liver, kidneys and suprarenals must hold back a small amount of the quinine for a long time. Doubtless, also the puerperal uterus retains quinine for a long time, for 2-5 days after injection labor pains were observed. For seventy years quinine has been administered to bring on labor pains with variable results. "Quinine is a capricious medication." In numerous experiments on puerperal cats it could be shown that 25, 50, 100 and 200 mg. of quinine injected intramuscularly, paralyzes the uterus until, either by secretion or destruction of alkaloids, the optimum of concentration is attained in the organism; then severe pains ensue. If one inject 1 mg./kg. quinine, after 1-2 hour, uterus contraction occurs. After intravenous injection of ½ mg. quinine per cat, labor pains are observed. Quinine is a toxin dependent on time. One must indeed agree that up to the present too much quinine has been administered to aid labor pains in human beings (repeatedly 0.3, 0.75-1.0 gm.!) 60 mg. is sufficient for muscular injection. Quinine sensitizes the uterus against mechanical and chemical influences.

On the Pathogenesis and Therapy of Psoriasis. — Erwin Pulay. (*Deut. med. Wochenschr.*, 55 : 1175, July 12, 1929.)

The works concerned with the question of the pathogenesis of psoriasis after endocrine impetus are numerous. An average type of constitution with definite administration of incretion substance did not work out well. Greater interest would be attached to the function of the thyroid gland except that an individual standpoint is incurred. The Abderhalden reaction on the pancreas, suprarenals, thyroid gland, liver and spleen gave diverging results. The rôle of the generative glands is also particularly discussed. Here, too, there is no regularity. Clinical observations often show either exacerbation or amelioration at the time of the menopause or at puberty, etc.

"In order to approach the problem with some sort of exact method, I made systematic investigations on metabolism. On the

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whole my observations were presented in three groups: those related to the hypothesis of depressed function (indication for thyroid gland therapy), those related to the hypothesis of increased function (contraindication of thyroid gland therapy) and those related to the hypothesis of depressed function and intense specific-dynamic albumin effect."

The divergent results must be referred to another gland incretion.

Cases of specific-dynamic albumin reaction permit the consideration of the possibility of disturbance of the pituitary gland. Yet, it could not be presumed that there was any causal relationship on this score. Upon reconsideration of the observations the fact becomes evident that in no case of psoriasis is there a normal process of metabolism. The endocrine disturbance seems to be closely connected with it. Upon application of the Abderhalden reaction this assumption seems to be further strengthened. In the first place the pancreas was exhausted.

The intense decomposition of the pancreas bears a definite relation to the voluminous information on the activity of insulin in psoriasis, and further, it is of particular interest in view of the very evident hyperglycemia, and finally in the frequent appearance of pancreatic disturbance in the intestines of psoriasis patients. From this viewpoint the foregoing, apparently heterogeneous conclusion derived a definite importance on account of this one fundamental distinction. The hormone correlation which exists between the pancreas, on the one hand, and the thyroid and pituitary on the other, suggested the consideration of metabolism. The functional adjustment in the pancreas in one case leads to rise and in another to intensification of the basal metabolism. The fact of the extensive interrelationship of secretion and incretion of the pancreas must be held fast. The pathogenesis of psoriasis points straight to a disturbed condition of the ferment.

Liver Therapy of Anemia in Nurslings and Young Children. — Jerachmiel Ligum. (*Monatsschr. Kinderheilk.*, **43** : No. 6, 1929.)

In accordance with observations of the Basler Children's Clinic, in various anemic conditions, even in the anemia of premature birth, essential results were obtained with liver therapy. The result of treatment with liver is therefore not only confined to the anemia of adults. Liver therapy has, however, the disadvantage that in many children it meets with aversion and occasionally therefore incurs failure, even with careful dosage; this is particularly true in the case of prematurely born children. Either liver juice obtained from fresh calves' liver or calves' liver cooked in water and then finely pulverized and mixed with the midday meal was given. We began with very small doses, in nurslings and prematurely born children the liver juice was administered in drops (20-40 drops three times daily). Results were obtained at first with large doses (20-80 gm. liver substance daily). The optimal amount was 15 gm. of liver substance for a kilogram of body weight, per day. This amount had scarcely any effect on the children. Good results were also obtained with Merck's liver powder. Dosage began with 1 gm. daily and was increased to 25 gm. The anemia decreased in about 4 weeks with liver treatment. The well established iron therapy must not be surrendered, however, to the liver therapy.

Labor and the Puerperal State.—W. Lahm. (*Geburtsh. Rundschau Jahersk. ärztl. Fortb.*, **20** : 12, 1929.)

Hatzki reports from the Obstetrics Institute (Stroeder) in Hamburg concerning the results of the injection of pituitary substances in labor. Pituitary gives successful results in about 30 per cent and failure in about 60 per cent. One can thus attempt the injection in cases of premature birth only if no danger ensues for mother or child from the unsuccessful result; with very premature children the test fails entirely. The thymus extract obtained from von Temesvary was tested in numerous experiments and in general a favorable criticism was obtained.

The Therapy of Allergic Diseases.—van Leeuwen and Storm. (*Fortschr. Therap.*, **5** : 41, Jan. 25, 1929.)

The best symptomatic medium for the prevention or suppression of cases to be treated is doubtless adrenalin. It acts promptly and almost never fails. Besides, in all cases refractory to adrenalin all other asthma remedies, with the exception of morphine, fail. It is further to be noted that there is no inuring to adrenalin and no adrenalemia. Naturally, abuse arises, but the author observed this only in desperate cases, in which there was merely choice

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between the question of abuse of adrenalin or abuse of opium derivatives. The author maintains that in the treatment of all allergics it is desirable to supplement the attacks with adrenalin. In cases of long existing asthma with functional emphysema and ultimately with bronchitis, the adrenalin injection is to be considered as direct causal treatment.

Cell Formers and Cell Forms of the Blood. II. Experimental Studies on Blood Formers after Adrenalin and Thyroxin Injections. — W. Stockinger. (*Zeitschr. ges. exp. Med.*, **65** : 52, 1929.)

The action of the both hormones, adrenalin and thyroxin was studied by the author, and from this less stress was placed upon the numerous changes of the white blood corpuscles than on the morphologic peculiarities of the cell forms under the influence of the both hormones.

A schematic report on the action of both hormones on the formation of the blood was not possible on account of discrepancy in the reaction. In myxedema the anticipated increase in cells following adrenalin administration fails. The process of increase of leucocytes after adrenalin and thyroxin takes place by means of the appearance of new basophilic cell elements. Adrenalin and thyroxin are both capable of initiating the transposition of cells for oxidative metabolism or for augmenting it.

Ephedralin, a Combination Product from Ephetonin and Adrenalin (Paranephrin). — H. Kreitmair and M. Leffkowitz. (*Deut. med. Wochenschr.*, **55** : 480, 1929.)

Blood pressure test shows that the prompt, brief action of adrenalin and the slow lingering action of ephetonin can be combined for an index of efficacy. And in cases of asthma,



Hormotone is theoretically a specific type of therapy in dysmenorrhea, for it contains those endocrine substances elaborated by the body for the specific control of menstruation.

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in the struggle for breath in chronic bronchitis and in emphysema, the pre-eminence of the combination and the prompt and long persisting effect finds clinical acceptance.

Further Application of Exsanguinated Suprarenals. — E. Borschers. (*Der Chirurg*, **1** : 389, 1929.)

The author shows by massive supporting evidence that extensive infiltration of the soft parts results with the use of adrenalin and also in narcosis during operations; 30 to 40 drops of suprarenal stock solution may be added when applying 200-400-800 NaCl solutions to the infiltration of the soft parts. By this procedure many operations may be rendered bloodless.

Insulin-Like Substances from Bact. Coli and Anthrax Bacilli. — S. Breüer. (*Münch. med. Wochenschr.*, **76** : 741, 1929.)

The author has previously reported in 1926 that culture filtrates of *Bact. coli* injected into rabbits intravenously in doses of 4-6 cc., induced a sluggish though eventual lowering of blood sugar. Later the author has investigated special cultures of anthrax bacillus for glucokinin formation and has found that, estimated on similar quantities of culture, the yield of glucokinin, in contrast to that of *coli* and *subtilis* is at least four times greater. The simple heated shaking autolysate of the bacteria shows a decreased blood sugar action.

Concerning the Attenuation of the Toxicity of Adrenalin by the Hypotensive Substance of the Pancreas. — Vaquez, P. Gley and Kisthinios. (*Paris méd.*, **19** : 445, 1929.)

The authors present the fact that the hypotensive substance of the pancreas, which is different from insulin, possesses the capacity, when applied intravenously, to lower the toxic action of adrenalin in rabbits. It seems that this substance protects the animals from acute edema in the lungs induced by adrenalization.

Insulin Treatment of Hyperthyroidism. — Coffin and J. S. Losse. (*Bruxelles méd.*, **9** : 668, 1929.)

The results obtained by the author with insulin treatment are as remarkable as any could be from patients in whom every other therapy had failed. On the other hand, the insulin therapy was followed by years of improvement. Daily insulin injections of units effect a definite lowering of basal metabolism and a coincident increase in body weight, quieting of the pulse and extensive quiescence of the psychic state of the patient.

Discourses on the Disturbances of Arterial Blood Pressure. — C. Achard. (*Progrès méd.*, **57** : 637, 1929.)

Medical therapy of arterial hypotension is primarily concerned with the administration of adrenalin and for this purpose, adrenalin was diluted with sufficiently large amounts of common salt solution and injected subcutaneously. In very severe cases intravenous injection is to be preferred. The arterial hypotension of tuberculosis is likewise to be offset with adrenalin, but the treatment must be stopped at once if the sputum gives the least evidence of filamentous blood particles.

The Use of Acetylcholin in the Clinic and for Therapy. — Maurice Villaret. (*Monde méd.*, **39** : 459, 1929.)

As conclusions of three instructive case histories the author presents evidence of the diagnostic and therapeutic value of acetylcholin. He reviews his case histories, their peculiarities and the method of their treatment. Acetylcholin decreases the blood pressure by means of its action on the peripheral arterioles. Hence it can be administered advantageously in cases of arteritis obliterans. Twenty cg. are given intramuscularly, morning and evenings. In cases of arterial hypertension 10-20 cg. are given. In ophthalmology, acetylcholin is given to offset spasms of the retinal blood vessels with blindness. Finally it is used with success in a few cases of hemiplagic apoplectic seizure.

The Presence of the Hormone of the Anterior Lobe of the Pituitary in the Urine. The Zondek-Aschheim Pregnancy Reaction. — R. Brühl. (*Münch. med. Wochenschr.*, **76** : 818, 1929.)

The so-called Reaction 1 of Zondek and Aschheim gives evidence of at least two hormones from the anterior lobe of the pituitary gland. It is agreed that the existence of both these hormones, the one inducing the growth and maturation of the follicle and the other resulting in luteinization, is necessary for the undisturbed process of the female cycle, so that with the transference of one of

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these hormones, or with its deficiency, disturbances can arise, such as are common in the climacterium.

Extended Application of Suprarenin Anemia. — E. Borschers. (*Der Chirurg*, **1** : 389, 1929.)

Suprarenin can accomplish much more than has been recognized up to the present, and the author is convinced after a year of experimental investigation and test in the operating room, that this medium can in no wise be substituted. There are only a few instances in which — though often only slight — a need for bloodless condition induced by suprarenin is not to be desired and the various possibilities of application are surprising if, preceding each operation, one asks oneself if it is not necessary for the patient and agreeable for the operator to operate bloodlessly. The author has performed bloodless operations in prostatectomy, large umbilical hernia and scar rupture, ureterotomy, resections of the tongue and the floor of the mouth and the Whitehead operation for hemorrhoids, without a single ligature, without loss of blood and without hemorrhage thereafter. Nephrectomy, radical operation of mammary cancer, resection of the bladder, operations on the spinal cord, in the region of the hip joint, can be operated upon with relatively few ligatures by this method. Extensive operations in the thorax lose some of their dreadful aspect if saturations are applied in and around the flaps of the soft parts. The author is definitely convinced that the so-called operation shock in severe cases will be greatly reduced if not suppressed, if the loss of blood is checked or decreased. The application of suprarenin is also very useful in the case of children.

In inflammatory processes suprarenin can only be valuable if there is a case of circumscribed disease condition, which can be surrounded by a suprarenin coating in healthy persons.

The fact can not be contested that checking of the blood flow and shortening the operation (by the absence or decrease of ligatures) often becomes a life-saving factor.

The Therapy of Epileptiform Symptom Complexes. — Max de Crinis. (*Mitt. Volksgesundheits.*, No. 4, 101, 1929.)

The study of metabolism and internal secretions has been a stimulus to the treatment of epilepsy by means of organ preparations. Bolton has given fresh expressed juices of thyroid and parathyroid rectally, it is stated, with good results. The author has found thyroid tablets also effective in a few cases. These results with thyroid gland preparations will perhaps be intelligible, since in epileptics there is often present an aplasia of the thyroid gland.

Concerning the Modern Treatment of Rheumatism. — Ernst Freund. (*Mitt. Volksgesundheits.*, No. 4, 118, 1929.)

For medical therapy the hormone is mentioned. The most common to be administered are ovarian and thyroid gland preparations. Concerning the latter, emphasis must be placed on the fact that it possesses not only a hormonal action but also a pharmacological action, so that a conclusion as to the etiology can not be drawn from the therapeutic result.

Results of Acetylcholin Treatment of Lead Colic. — Laignel-Lavastine and Jean Fouquet. (*Progrès méd.*, 520, 1929.)

A 30 year old workman who suffered a sudden severe lead colic was treated with acetylcholin, whereupon the colic pains disappeared. Simultaneously obstipation vanished with the pains and abdominal retraction, arterial hypertension and vasoconstriction disappeared also.

Action of Acetylcholin on Glycemia. — M. Labbe, F. Nepveux and L. Justin-Besançon. (*Paris méd.*, **19** : 316, 1929.)

The injection of 20 cg. of acetylcholin fairly regularly causes a decrease of glycemia, which, however, incurs individual variations. This decrease can be intense and of long duration in healthy persons. In certain forms of diabetes and obesity it seems rather intense.

Concerning the Treatment of Coma Hepaticum, Especially with Regard to Injury to the Liver Parenchyma, in the Course of Gallstone Troubles. — G. E. Konjetzny. (*Zentr. Chir.*, **56** : 770, 1929.)

The author obtained favorable results in two cases of very severe cholemic condition with insulin-grape sugar treatment used by Umber and Richter, and he therefore held it obligatory, in similar cases, to test the effect of insulin-grape sugar treatment in each instance. (1000-2000 cc. of a 5 per cent solution of grape sugar per day, and to each 2.3

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gm. of grape sugar a unit of insulin.) The premise for the undertaking is generally the presence of some efficient liver parenchyma. The symptomatic value of grape sugar-insulin treatment in carcinoma of the liver is also emphasized. The painful symptoms which accompany this condition will be actively combated.

Pituitary and the Law of Puberty. — A. Lipschütz, H. Kallas, and R. Paez. (*Pflügers Arch. ges. Physiol.*, **221** : 695, 1929.)

The anterior lobe of the pituitary of castrated guinea pigs acts the same on the genital organs of infantile mouse as does normal pituitary. The action still occurs even after a year's castration on the part of the donor.

The uterus is also affected by the administration of pituitary of young or infantile animals.

In positive cases the effect in the ovary after administration of pituitary from either an adolescent or an infantile animal can be determined.

Likewise after the injection of pituitary of a 14 year old senile dog changes occurred in the uterus and ovary.

The report of Smith and Engle, that the anterior lobe of infantile animals secretes hormone and that that of old animals still produces it, is confirmed.

Concerning Several New Medicaments. — René Hazard. (*Bull. méd.*, **43** : 381, 1929.)

According to the latest experimental investigations it appears that actually there is agreement between natural thyroxin and synthetic thyroxin (identity) and that hyperthyroxination induced in animals of various sorts is the same as a condition of hyperthyroidinization. Thyroxin administered *per os* gives the same results with respect to appearance and duration as thyroid gland extract. One mg. of thyroxin is really about the same as 0.20 gr. thyroid gland extract.

Ovarian Hormone, Insulin and Carbohydrate Metabolism. — E. Kaufmann. (*Deut. med. Wochenschr.*, **55** : 650, 1929.)

The ovarian hormone affects carbohydrate metabolism in the exact opposite manner of insulin. On this basis are explained the sensitivity of children to insulin, the danger of hypoglycemia in diabetic puerpera, the slight decrease of carbohydrate metabolism in the ovarian cycle and in the process of pregnancy in diabetics.

The Therapy of Nephrosis with Liver Extracts. — L. Rohácek. (*Zentr. inn. Med.*, **50** : 337, 1929.)

By nephrosis the author understands the symptom of Volhard's genuine nephrosis, not the various sorts of "nephrotic complexes." In a patient with edema in whom the therapy with urea was unsuccessful, he first tried a therapy with kidney and liver extracts, based on the idea that in the kidney and liver there might be a regulatory substance which might have an effect on the assimilation of water and also on the metabolism of salt. First the patient received only renin injections, later alternating renin and hepatin injections (for 4 months). The symptoms of edema did not occur from the time of the hepatin injections. Likewise the hypercholesterinemia entirely disappeared. The author also investigated the effect of the therapy on other patients. In nephritis, and such cases, also, as nephrotic degeneration, the remedy did not have a lasting effect.

Regarding the hepatic activity in patients afflicted with liver diseases the author found that hepatin facilitates the removal of chlorides from the tissues into the blood. In atrophic cirrhosis the action of hepatin is only superficial and it is not possible to cure the cirrhosis with hepatin.

Pituitary and Genital. — J. Novak. (*Med. Klin.*, **25** : 643, 1929.)

The active substance which induces the changes in the ovary is contained in the anterior lobe of the pituitary, alike in infantile and senile animals. The action of the anterior lobe on the accessory sex characters is only possible if the sex glands are included, so that the pituitary is correctly considered as the initiator of sexual function. The active substance of the anterior lobe is water-soluble but not lipoid-soluble. It is not an albuminous substance, and is very sensitive to heat, acids and alkali. As mouse unit the amount used was that which brought about in 100 hours, in a mouse weighing 6.8 gm. the characteristic changes in the ovary, and initiated estrus. The rat is much more sensitive than the mouse. In pregnancy the pituitary produces much more hormone than formerly. This hormone is evident in the urine, in the placenta and in the blood in large quantities

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The author was successful in bringing back the menses in a case of amenorrhea, but he emphasizes the disadvantages of dosage and the causal analysis of the disease symptoms. However, the hormone of the anterior lobe of the pituitary ought to be tested on genital hypoplasia and in premature involution. The reports of results in experiments on animals and human beings are vastly different from each other. There is no evidence of efficacy in childhood or in the climacterium, although the pituitary produces hormone in these periods, also. Further, the author hopes that the administration of the hormone of the pituitary will become as important as the administration of thyroid and insulin.

Investigations on the Hormonal Activity of the Anterior Lobe of the Pituitary of the Fetus in Animal Experimentation. — F. Schultz-Rhonhof and R. Niedenthal. (*Zentr. Gynäkol.*, **53** : 902, 1929.)

The authors implanted the pituitary of a human fetus in animals and three sexually mature castrated mice and eighteen infantile animals each were implanted with an entire pituitary. Two infantile mice were each implanted with two whole pituitaries.

From this it was seen that in none of the cases was the ovary entirely unaffected, although the changes were often only slight. Also in almost all the cases the secondary reaction of the vaginal orifice is evidence of the fact that the hormone of the anterior lobe of the pituitary must have expanded its action first in the ovary. The finding of the author settles the contested problem of whether hormone of the anterior lobe of the pituitary of human fetus produces the hormone stimulating ovulation, affirmatively. In tests with the anterior lobe of the pituitary of fetus cortex, it is evident that a production of the hormone influencing ovarian function is also present in the animal fetus.

Observations on the Fall in Temperature Directly after an Insulin Injection in Two Cases of Protracted Increase in Temperature. — A. Puech. (*J. practiciens*, **43** : 833, 1929.)

For the purpose of increasing the appetite and improving the general condition, an insulin injection was made in a patient who for more than a month had had a temperature between 38° and 39°, and in whom no basis could be found for the height of temperature. The temperature fell promptly to 37.5° and after 3 days a total recovery of the patient was obtained. Fifteen units of insulin were injected in another case in which, for ½ year the temperature stood between 37° and 38° and every therapeutic attempt had been unsuccessful. On the day immediately following the patient was free of fever and remained so. Though unable to explain the mechanism of recovery in these two cases, the author thinks that the matter was not one of entirely accidental occurrence.

Concerning the Mode of Action of the Thyroid Gland Hormone. — Weil, R. Landsberg and M. Landsberg. (*Biochem. Zeitschr.*, **207** : 186, 1929.)

The authors undertook investigations in order to study the processes involved, especially in the albumin metabolism of thyroxin, above all in the liver as the chief place of all metabolism, and have tested the influence of thyroxin on the autolysis of liver broth (guinea pigs). The autolytic process shows a synonymous increase of the mechanical destruction of tissue structure, independent of the pH of the medium, a slight increase also with substances other than thyroxin.

The point of view concerning change in water-salt metabolism under the influence of thyroxin is in accord with the theory of permeability of thyroxin activity. The wandering off of electrolytes from the tissues into the blood is certainly the primary process in the diuretic effect of thyroxin. Consequently, the thyroxin induces a better distribution of electrolytes. It is doubtful whether thyroxin calls forth increased tonus of the autonomous nervous system. The experiments of the authors show that thyroxin, in dilution to 1:400,000 quantitatively furthers the tissue autolysis by neutral reaction. As an outcome of this observation the authors sought to explain consistently the manifold metabolic effects of the hormone of the thyroid gland on a physico-chemical basis, that, since each stimulation induces further permeability of the plasma membrane, it is theoretically possible to increase or inhibit, simultaneously, by hormone or nerve, the identical or contrary effect on the cells.

The Heart Hormone. — Zuelzer. (*Med. Welt*, **3** : 511, 1929.)

The author reiterates that he doubts the hormone nature of the substance designated

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by Haberlandt as heart hormone. Haberlandt alone is responsible for the proof of the hormonal nature of his substance. This fact is all the more difficult to prove, as has been said at the Vienna Conference for Internal Medicine, for many chemical substances have the same effect on the frog heart as the heart substance of Haberlandt. Since the frog heart has no coronary arterial system, it is particularly inappropriate and unnecessary to draw conclusions concerning its reaction to the activity of a hormone. To this end convincing experiments on mammals must be undertaken.

Female Sex Hormones. Contribution to their Experimental Study. — F. G. Triviño. (*Med. Ibera*, **21** : 225, Sept. 17, 1927.)

The serum from pregnant women produces in infantile rats, that is, in rats with genital organs still immature, in addition to initiation of the estrous cycle, a marked increase in size of the uterus. The active substances proceeding from this serum are thermostabile, soluble in alcohol and apparently diffusible.

The content of these substances per cubic centimeter is 10 biological units and as site of their production the quantitative content of the ovary in these substances can not alone be taken into account. Probably the placenta and perhaps the uterine wall contribute to their production.

Clinic and Therapy of Arterial Hypertension. — J. Pal. (*Med. Klin.*, **24** : 160, 1928.)

Several authors have described a lasting blood pressure-lowering effect of certain liver extracts.

The author carefully tested various preparations of the type, clinically as well as experimentally, but without exception in all cases he had to record unsuccessful results with these preparations.

Concerning Liver Extract Treatment of Pernicious Anemia. — Seyderhelm and G. Opitz. (*Klin. Wochenschr.*, **7** : 205, 1928.)

Every speculation concerning the true nature of the active liver substance, in particular every discussion whether it is a question of a vitamin or a hitherto unknown hormone, must remain without purpose as long as it has not been possible to free the specific active principle of the organ and investigate it experimentally and biologically. In the follow... a report will be made concerning a liver fr... tion analogous to that prepared by Minot a... Murphy with Cohn. Analysis of this extra... gives: N: 7.8 per cent, P: 3.4 per cent, Fe... traces, S: 0.015 per cent, NaCl: 1.46 per ce... Alb. Peptone, Polypeptide: (+). As a rul... the patient with pernicious anemia was give... as much liver extract as corresponded to th... amount of 400-500 grams of fresh liver, the... is 7.5 grams of the desiccated substance and... 80 grams of the fluid substance, that is, about... 4 tablespoonfuls. The effect of the liver... extract on pernicious anemia is effectively... the same as is attained by administration... of liver. It appears that later after attain... ment of the normal blood count one can go... back to an amount of extract corresponding... to 200 grams of fresh liver. It is remarkable... that also after administration of liver extract... in the majority of cases the change in sub... jective condition as well as in blood picture... sets in already within the first week of treat... ment. Almost regularly an increase in... leucocytes appeared simultaneous with the... slow rise in hemoglobin and erythrocyte... count. Instead of leucopenia with relative... lymphocytosis and deficiency of eosinophil... cells, an increase in neutrophil leucocytes... appeared, for the most part accompanied by... a rise in eosinophil cells. Moreover, in the... majority of cases — very frequently even... during the first week of liver extract therapy... — occurred the retrogression of urobilinogen... and urobilin as well as indican in the urine... In other cases, the improvement introduced... by means of liver diet proceeded entirely... similar upon transition to liver extract treat... ment. In three patients examination of the... gastric juice following liver extract treatment... showed the disappearance of colon bacilli... always present in quantities before treatment... The demonstration of colon bacilli in the... gastric juice in pernicious anemia is so regular... a finding that diagnostic significance may be... ascribed to it.

The reappearance of hydrochloric acid... production of the stomach observed in one... case of pernicious anemia following liver... extract treatment was most striking. This... single observation shows that with liver... therapy actual lost functions in the sphere... of the intestinal tract may be restored. With... all precaution it should be declared that the... observations made allow the possibility of a... primary influence of liver extract on the intes...

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...nal functions to appear disputable. Finally, it must also be mentioned that even in hypochrome "secondary" anemias, striking successful effects were observed with liver extract; of course, such cases in practice are treated as well with iron or arsenic. An eventually refractory course would justify a trial of the costly preparation — whether it be daily feeding of liver or liver extract. Moreover, actual observations show that a special importance likewise falls to the share of liver extract in anemia complicated by renal disease. In a case of severe secondary contracted kidney with a high degree of anemia and leucopenia, the latter symptom reacted within a few days to administration of liver extract in analogous manner to the leucopenia of pernicious anemia. The leucocyte count rose from 4000 to 10,000, the eosinophils, which were previously altogether wanting, appeared up to 6 per cent. The significant intestinal autointoxication manifest in nephrosclerosis is apparently influenced in like manner by treatment with liver extract, as in pernicious anemia.

The Active Constituent of Glukhorment. — H. H. Dale and H. W. Dudley. (*Brit. Med. J.*, No. 3491 : 1027, 1927.)

Through very careful chemical test and analytical study it was determined that the substance isolated from glukhorment may not be differentiated from the synthalin prepared by Kahlbaum with the methods used. It is either identical with synthalin or so intimately related that laborious chemical analyses with great amounts of material would be requisite for their investigation. Physiological investigations on rabbits showed that the glukhorment tablets, as they were prepared for therapeutic purposes, either contained synthalin itself or a substance so closely related to synthalin that it could not be differentiated from it by the chemical and physiological methods used. Glukhorment contains this substance in sufficient amount to play an important rôle in any therapeutic or other activity. Concerning the therapeutic value of glukhorment, the authors can give no decision.

Results of Dietetic Treatment of Pernicious Anemia. — R. Seyderhelm. (*Klin. Wochenschr.*, 7 : 1, 1928.)

Organotherapy with liver appears to surpass all therapeutic measures hitherto undertaken for the cure of pernicious anemia. Minot and Murphy are inclined to assume, on the basis of their extensive observations, that liver diet in the treatment of pernicious anemia has the significance of a specific, curative therapy; that it is a question of causal therapy. Minot and Murphy place pernicious anemia parallel to actual avitaminosis in which a causal significance falls to the share of preceding defective nutrition. With regard to the action of liver they come to a like conception as Whipple, according to which an important building material is supplied to the stromata by liver, that is, the supporting substance for the erythrocytes. As actual cause of the pernicious anemia they conceive of a primary disturbance of bone marrow function. With regard to the nature of the active liver substance, Minot and Murphy do not believe that the vitamin E found in the liver by Simmonds, Bekker and McCollum (which is important for the metabolism of iron) is the principle curative of pernicious anemia. Whereas vitamin E is insoluble in water, the liver substance influencing pernicious anemia proved to be soluble in water, precipitable in alcohol, and insoluble in ether. It is free from lecithin, and lipoids, and contains approximately 7 per cent nitrogen, slight traces of albumin and sulphur. The ideal form of liver therapy is, to be sure, the administration of a liver extract which contains the active liver principle. In liver therapy the mechanism of action is still to be determined. It is possible that a substance regulating blood formation, a blood-forming hormone, is present in the liver.

Treatment of Senility and the Dynamogenic Effects Observed in Man by Ingestion of Activated Serum of Young Male Animals. — Ch. Levassort. (*Progrès méd.*, 4 : 160, Jan. 28, 1928.)

The author reports the result of his experiences with M. Busquet's serum in old age. This physiologist has already published the account of the effects of induced masculinization on old roosters and capons by a special serum of young bulls, containing both the circulating hormones of young animals and the antibodies of inhibiting substances discovered by A. Carrel in senile organisms. Ch. Levassort has noted that when administered by mouth 30 minutes before meals, in a dose of 20 cc. per day, the activated bull serum produces in certain depressed individuals and in old people of both sexes, effects of invigoration

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manifested by a greater aptitude for physical and mental work, by a feeling of well being and an optimistic change in disposition.

Insulin Treatment of Diabetic Addison's Disease. — W. Umber. (*Med. Klin.*, **24** : 8, 1928.)

Report concerning clinical experiences in 2 cases of suprarenal disease which were complicated by diabetes without rendering insulin therapy more difficult; moreover, insulin treatment could be carried on without danger of hypoglycemia and with the same dosage as in diabetics with intact suprarenal glands. In the one patient, it was a case of moderately severe diabetes and typical Addison's disease; the second case was that of a diabetic patient with pulmonary tuberculosis and Addison's disease. This case demonstrated in its course that the principle of hyperinsulinization, as it is used for tuberculous diabetics, can also be successfully employed in diabetics with pulmonary tuberculosis and Addison's disease. In all cases, however, it is recommended to introduce the insulin dosage carefully and slowly, in order that an eventually existent insulin sensitiveness such as Unverricht published can be taken into account. The fact that diabetic Addisonians tolerate just as high a dosage of insulin as diabetics with normal adrenals, is not to be explained without further ceremony. It appears as if a compensatory rise of adrenalin production is still possible through hypoglycemia, by which on the one hand the lack of threatening sequelæ of the hypoglycemic symptom complex, on the other hand, also the simultaneous pronounced rise in blood pressure associated with slight hypoglycemia find their explanation.

The Mechanism of Action of Synthalin. — F. Bertram. (*Deut. Arch. klin. Med.*, **158** : 76, 1927.)

Report concerning the author's clinical experience with synthalin in 21 diabetics. In mild to moderately severe cases there resulted an influence on hyperglycemia and glycosuria at the outset. Dyspepsia could be avoided in almost all cases by the use of lecithin-cholic acid. After longer use of the preparation there occurred, however, in the majority of cases a deterioration of the metabolic state. In severe cases of diabetes a favorable influence on the metabolic condition could not be determined in any case. In many cases a marked primary hyperglycemia succeeded even relatively small doses. In three cases precomatose conditions made their appearance with the addition of synthalin and continuance of the therapy employed up to that time (diet and insulin). Following discontinuance of synthalin in the greater number of severe cases of diabetes which were treated with insulin, a similar deterioration of the metabolic condition was noted, so that for the maintenance of the earlier existant equilibrium much higher amounts of insulin than previously were requisite. Severe pains in the vicinity of the liver appeared four times in the course of the treatment. Through experiments on man it can be shown that the blood sugar-lowering action of synthalin takes place through the pouring out of insulin from the pancreas — therefore in the sense of a parasympathetic poisoning. With the administration of sufficiently large amounts of atropin it is possible to weaken the blood sugar-lowering action of synthalin in diabetics, or to entirely destroy it. Instead of this in many cases a marked primary hyperglycemia is observed. Atropin may in individual cases considerably lower the renal threshhold for sugar, so that with examination of the urinary sugar alone, an improvement in carbohydrate tolerance is simulated.

Whereas during the administration of insulin in the diabetic, an extensive sparing of the island apparatus and glycogen deposition are obtained, following synthalin a stimulation of the pancreas ensues and with it exhaustion of the organ which is already damaged. The primary effect of mobilization of blood sugar conditions a decrease of glycogen supplies in the organism. The possibility is discussed that the decrease of glycogen stability, the icterus observed by many authors and the yellow dystrophy of the liver observed by the author merely represent different degrees of a liver poisoning by synthalin. The use of synthalin even in mild and moderate cases is also warned against.

Neuro-Anemic Syndrome. Remarkable Therapeutic Effects Obtained by Whipple's Method. — Crouzon, P. Mathieu and G. Dreyfus. (*Paris méd.*, 17 : VIII. Sept. 10, 1927.)

A new case of neuro-anemic syndrome is reported with spasmodic paraplegia, profound disturbance of sensibility, mental phenomena and cryptogenetic pernicious ane-

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mia. Under the influence of the daily ingestion of 250 grams of boiled calves' liver and exclusive of all other treatment, the asthenia and digestive troubles progressively disappeared; weight increased 7 kilograms, and the number of red blood cells increased from 1,750,000 to 2,800,000 to about 5,000,000. The authors stress the remarkable effects of this new therapeutic method which within 4 months has transformed a bedridden invalid into an individual capable of leading a normal life.

Practical Therapeutics

(*Continued from page 210*)

enzymes, digests albumin bodies, therefore, decomposes dying tissue in a wound not healing by primary intention, that is, it leads to wound cleansing and consequently to healing.

At St. Catherine's Hospital, Surgical Department, in the last 4 months, Roehm's enzyme preparation was used in a great number of cases. Of this number several cases in which a particularly striking effect was obtained with the enzyme preparation are reported:

(1) 62 year-old patient with greasy coated, large ulcers of the leg, which were treated without success with the most varied remedies. The wounds were finally treated with enzyme powder and rest in bed and already with the second change of dressings, the reactive inflammation had disappeared. Then increased secretion of the wound set in; following further powder treatment rapid cleansing, healing over and after 4 weeks the patient was discharged cured. Also in a number of other patients with ulcera cruris favorable experiences were had with the enzyme preparation. Usually powder treatment was used first, and following cessation of the secretion, ointment treatment. Especially good curative result was attained in a decubital necrosis of the scrotum as large as the palm of the hand in a strikingly short time. There is now present only an epidermis defect as large as a cherry; the patient will probably be discharged as cured within a week. Likewise a furuncle was healed very rapidly under enzyme treatment, after it had resisted every form of therapy for weeks. In incised whitlows, furuncles and abscesses, the enzyme ointment promoted wound cleansing to such an extent, that the time of treatment was much shorter than with the use of other therapeutic agents. Greasy, covered and soiled contused wounds are suitable for treatment with enzyme ointment. Frequently such wounds cleanse their wound bed in a very short time and heal up. The action of the enzyme preparation was also very striking in a patient with extensive second degree burns on the face and on both hands. They were treated exclusively with enzyme powder which was dusted on thickly. Also here at first increased secretion appeared, giving place soon to a fresh appearing granulation surface. In a very short time cure resulted, more quickly than would be expected. In any case, it may be said that the experiences which were had with enzyme treatment were good throughout.

Pernicious Anemia of Pregnancy. Treatment by Whipple's Method. — P. N. Deschamps and A. Froyez. (*Bull. et mém. Soc. méd. Hôp. Paris*, **52** : 143, Feb. 9, 1928.)

Pernicious anemia of pregnancy has always been considered one of the most severe forms of anemia. The patient, a woman of 27 years, in the sixth month of pregnancy, entered the hospital on July 22nd, with a typical syndrome of severe anemia and a blood count of not more than 1,800,000. She ingested 250 grams of cooked calf's liver daily from July 25th to August 17th. During this period the blood count rose from 1,800,000 to 5,000,000 and all clinical signs of anemia disappeared. From August 20th to N v. 11th, even though no hematopoietic treatment was instituted, the number of red blood cells did not fa l below 4 000,000.

On October 31st, the patient was delivered at term, under normal conditions, of a living child as well as of a mummified fetus. From a clinical point of view, such an anemia would appear to enter into the class of pernicious anemias of pregnancy. In this case, the onset of the disease occurred insidiously in the first months of pregnancy, the severe symptoms made their appearance towards the sixth month, with appearance of edema, albuminuria, the hematologic picture of plastic anemia, with but slightly marked myeloid reaction and slightly increased leucocytic reaction, accompanied by a tendency to polynucleosis. The authors stress two points in particular: (1) The patient was a primipara, whereas the majority of cases of pernicious anemia of pregnancy occurred in mul-

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tipara. (2) The menses had persisted up to the fifth month.

The evolution of the anemia in this patient differed entirely from the usual course of pernicious anemia of pregnancy. All observations agree in confirming the impossibility of a remission, whatever the treatment instituted may be, so long as the fetus has not been expelled. To the authors' knowledge, there does not exist a case of pernicious anemia of pregnancy in which the blood count rose before delivery. The authors, accordingly, undertook the treatment of such a case by Whipple's method without great hope. Being familiar with the usual absence of any improvement before expulsion of the fetus, they did not dare to employ Whipple's method alone. To it they added the classical treatment of pernicious anemia by transfusion. It appears impossible, however, to attribute the principal effect in the present case to transfusions. The blood cell count increased remarkably (within 29 days the number of red cells increased from 1,800,000 to 5,000,000 in order to continue at 4,000,000 3 months later). It is to be noted that this therapeutic action of calf's liver occurred here in a severe anemia, to be classed among the symptomatic anemias, whereas in the primary opinion of American authors, the method in question would be truly effective only in cryptogenetic pernicious anemia of Biermer's type. This case would seem to represent an argument of great value in favor of the efficacy of liver therapy in the treatment of severe anemias.

Thyroid Insufficiency, Plethora and Polycythemia. — J. García G. Morán. (*Siglo méd.*, **80** : 223, Sept. 3, 1927.)

The patient was a woman aged 58 years. Her menstrual history was normal, although menstruation tended to be profuse. Menopause occurred 18 years ago. Five years ago, following an attack of grippe which necessitated rest in bed for 3 months, the patient noted swelling of the legs, then generalized swelling and tendency to sleepiness. Examination showed intense somnolence. The patient fell asleep everywhere; she was very obese, with spongy appearance and great abdominal plethora; skin, dry and scaly; hands, cold; basal metabolism −27; red blood cell count, 6,120,000 per cubic mm.; weight, 100 kilograms, 300 grams; hypertension; constipation. A diagnosis of thyroid insufficiency was made, with plethora and polycythemia and the following treatment prescribed: two 0.3-gram tablets of thyroidin, daily, with dietary restrictions. Following several months of treatment, the patient showed marked improvement: loss of weight to 83 kilograms; somnolence no longer present; basal metabolism had risen to +5; red blood cell count amount to 3,090,000 per cubic mm.

It is very probable that the case was one of a syndrome of thyroid insufficiency in which the physical appearance and somnolence were the main symptoms. Constipation and profuse menstruation are also symptoms of hypothyroidism. The hypertension appears to be essential; renal function was perfect. Following thyroid treatment to which all other symptoms responded, only hypertension remained unchanged.

The action of thyroid medication on the polycythemia was especially noteworthy in this case. Two months of treatment resulted in a decrease in number of red blood cells from 6,120,000 per cubic mm. to 3,090,000. In this case it is evident that the polycythemia disappeared when the hypothyroidism and plethora had been remedied. Hence, the action of thyroidin in cases of hypothyroidism in which there is polyglobulia is an indirect one and this latter symptom disappears only when the plethora has vanished.

Acid Base Equilibrium in Addison's Disease. — G. Marañon and J. Morros Sardá. (*Siglo méd.*, **80** : 197, Aug. 27, 1927.)

Knowledge of the changes in the blood of Addisonians is increasing daily. Thus, it is well known that these cases are usually accompanied by hypocholesterinemia; that the leucocyte formula changes in the sense of a marked lymphocytosis: the rate of sedimentation of red blood cells is very much accelerated; the blood sugar curve usually reaches low values, etc. It appears, however, that the acid-base equilibrium in these patients has never been studied. The authors examined six Addisonians in this respect and in four of them they found a manifest fall of the alkalin reserve, which consequently revealed a state of acidosis. In the remaining two cases, they encountered values near normal but which also indicated a tendency towards hypoalkalinity. From the study of these cases, they deduced that the fall in alkalin reserve maintains an evident relationship with the intensity of the general disease pic-

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sure, since the reserve was especially low in the patients with most pronounced symptoms and reached almost normal figures in the two patients whose condition was relatively satisfactory.

It is difficult to interpret this acidosis in Addison's disease. It is possible that the tuberculosis infection plays a rôle in these disturbances of the acid-base equilibrium due to the phenomena of proteolysis to which it gives rise. The state of malnutrition in which these patients are found, especially in advanced cases, might also be a factor in the genesis of the acidosis. Another possible explanation would be the retention of poisons of muscular origin which when incorporated into the humors of the body would tend to vary its reaction. Abelous and Langlois and a great number of physiologists and pathologists (Zondek, Pende, etc.) admit that the suprarenals normally destroy or neutralize toxic substances resulting from muscular contraction. As these products are mainly of acid nature, the authors believe that they might be the cause of the acidosis in question. At any rate, the existence of this disorder in Addisonians might serve to explain the poor resistance of these patients to surgical interventions. These facts suggest a trial of alkalin therapy in Addison's disease, especially in advanced forms when acidosis is manifest. Insulin should not be used for this purpose in these cases, because of the extreme sensibility of Addisonians to this medicament, unless great quantities of glucose have been administered previously.

Extension of the Field of Therapeutic Liver Diet. — M. Grossmann. (*Med. Klin.*, 23 : 1851, 1927.)

A patient with most severe cachexia, considerable edema, inability for active movement, severe anemia of hyperchromic type and an amount of urine of 400 to 600 cc. was treated with liver therapy after an unsatisfactory trial of Salyrgan (only transient result and causing headaches), theobromine preparations (without effect) and urea (effective, but causing vomiting). Diuresis rose to 1500 cc. and remained at this level for a long time; it now amounts to 1200-1500 cc. Excretion of sodium chloride rose from 2.5, 2.7 to 4 and more per day. To be sure, it showed variations. General condition is good, but there is still no complete recovery, since in the urine cylinders and albumin are present even if there are no more lipoids. The observation speaks in favor of the presence of hormones in the liver. Probably there exists a primary similarity between the effect of the liver on diuresis and thyroidin action.

Johannes von Kries

(*Continued from page 212*)

thought processes of others and his ability to express the splendid ideas he found made his work on "Goethe as a Psychologist" (1924) and on "Immanuel Kant and His Significance for Natural Research of the Present" (1924) worthy of high praise in the realm of criticism. Likewise his interpretation of the work of von Helmholtz ("Helmholtz as Physiologist," in *Die Naturwissenschaften*, 1921) is commemorable. The task of commenting on all the individual writings of von Kries is far too great to be undertaken in this place. The few that are mentioned give an insight into the many phases of his capabilities. Von Kries was not only a prolific writer but a profound one, also. He was a man of few words, and mighty ones; one of his pupils reports that "A short discourse brought us work for weeks to come." He was always a helpful, inspiring leader, anxious to progress to the last limits of a problem, or at least as far as was humanly possible, and to leave it finished thus far so that his followers might take up threads and go on. He proceeded cautiously but surely, not following a battle cry, for he despised showy pretense, but with feet firmly based on the truth and mind alert for all possible contingencies and capable, through its own dominance, of interpreting man, his life and his thoughts.

Concerning Mastopathy of the Male Mammary Glands. — Moszkowicz. (*Münch. med. Wochenschr.*, 74 : 874, 1927.)

Observation of ten personal cases and the review of the literature showed that hormonal incitation is in evidence in diseases of the male mammary glands as well as in the female. Delayed maturing of the testis and premature involution can exert a profound effect on the mammary glands. Moreover, changes in the mammary glands are encountered in simultaneous insufficiency of the internal function of the testis, as well in constitutional (cryptorchidism, hypospadias) as in acquired inferiority (syphilis, tuberculosis, etc.). Finally the author regards the "intersexual individuals" as disposed to mastopathies.

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Eunuchoidism and High Pressure. — W. Seidel. (*Med. Klin.*, **23** : 652, 1927.)

The author describes two cases in which the most important characteristics of the symptomatology of eunuchoidism (Tandler and Gross) were present, namely, overgrowth of the extremities in proportion to body size, scantiness of axillary and pubic hair, with heavy growth of hair on head, genital disturbance and a pelvic formation resembling feminism. The author stresses the fact that the abnormal length of the extremities is not, according to his observations, *a priori* to be taken into account, but only in connection with other eunuchoid symptoms.

Concerning Insulin Shock. — O. Klien. (*Med. Klin.*, **23** : 1776, 1927.)

The course of reaction in insulin shock differs qualitatively and quantitatively in different individuals. Of the objective changes in insulin shock, insulin leucocytosis is especially interesting. It is variously strongly pronounced in different individuals, and always becomes weaker with repeated shock in one and the same individual. In diabetics previously treated with high insulin dosage, insulin leucocytosis also remains absent in very severe shock. In icteric patients, no leucocytosis could be observed in great shock for the most part from the beginning. The insulin leucocytosis is not influenced by the same factors as insulin hypoglycemia. Leucocytosis is set aside only by glucose; insulin hypoglycemia and leucocytosis as well as insulin shock were almost without exception increased by administration of a great amount of water (1.5 liters). Blood sugar fall and rise in leucocytosis followed in steep curves; shock was especially of long duration; likewise the descent of the blood sugar level. Administration of glucose set aside the shock here and the hypoglycemia, but only transiently. It is probably a question of strengthening of the parasympathicotropic action of insulin on the vegetative nervous pathways (effect of fullness of the stomach as vagus stimulus; strengthening of the liver contraction in insulin shock through these latter). In liver disease, the insulin shock is especially powerful and lasting in relation to insulin dosage, likewise the objective hypoglycemia. In liver disease, in insulin shock, the following observations were made: Fall of bilirubin picture often about 3-4 units, shortening of the time of coagulation of the blood, occasionally relative increase in fibrinogen and globulin fraction of the plasma-albumin substance. The thickening of the blood is especially intense in liver disease. Therapeutic use of the influence of insulin on liver activity: Richter observed prolongation of the life of a patient with acute yellow atrophy of the liver under insulin treatment. The author also observed the disappearance or decrease of icterus in the most varied liver affections (cirrhosis, hepatitis, etc.) lasting for months. The relation between insulin shock and change of acid-base equilibrium is not lawful. The alkalosis of the blood, when present, is rather to be regarded as sequel to the shock and not as the cause. In liver disease, for the most part fall of alkalin reserve, despite the most intensive shock with acid-urine reaction. In severe acidotic diabetics rise of alkalin reserve results in hypoglycemia, with shock very slight or altogether lacking. Here, for the most part, one does not succeed in obtaining shock despite hypoglycemia (often with very low blood sugar level) so long as the cholesterin picture of the blood remains high and a lipemia is demonstrable. The urine also remains acid in reaction for just so long a period. After several days of diet rich in carbohydrate, with high insulin dosage, removal of the hypercholesterinemia occurs. With the appearance of hypoglycemia — with normal cholesterin picture — the typical shock takes place, whereupon the actual reaction of the urine changes to alkalin. In two precomatose diabetics, hypoglycemia was systematically brought about daily through overdosage of insulin. As long as the cholesterin picture remained high, no shock occurred despite extreme fall of the blood sugar picture. The reaction of the urine remained permanently acid. First following several days of farinaceous diet with high dosage of insulin did typical shock with normal cholesterin picture set in, upon which the actual reaction of the urine also changed to alkalin (pH equals 7.6). In diabetics previously treated with high dose of insulin, likewise in genuine hydropic kidney disease, the alkalin reserve is for the most part relatively high, the actual reaction of the urine near the neutrality point; hypoglycemia and shock appearing especially mild here (with small dose); especially intensive shock, change in reaction of urine to alkalin, appearing according to law! In both cases alkalin enrichment of the organism exists.

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This favors the occurrence of shock; it is, however, not the direct cause and also not the necessary condition for the occurrence of the symptom. The origin of very intensive shock in acidotic liver disease speaks in favor of this, where the alkalin reserve falls in shock with urine reaction remaining acid, as well as in the acidotic patient with renal insufficiency, where with low alkalin reserve (for example, 18 per cent of volume) and strongly acid urine reaction (pH equals 4.5), violent shock was observed. With hypernormal position of the water deposit in the organism, strong diuretic effect is not infrequently noted in insulin shock (for example in edematous kidney disease; in diabetics previously treated with high doses of insulin). A diuresis of 4 to 5 liters and corresponding loss of body weight in 24 hours was more frequently observed. In two edematous renal patients (nephrosis), in whom otherwise diuresis could not be obtained in any way, complete removal of edema followed insulin shock. In addition to water, abundant alkali was also evacuated here. In one case the pH of the urine was 8.0 with an amount of urine of 3 liters.

The Hirschsprung Syndrome as the First Indication of Congenital Myxedema. Several Additional Observations concerning Megacolon Idiopathicum. — J. C. Schippers. (*Monatsschr. Kinderheilk.*, 43 : 289, 1929.)

A 5 year old girl with obstinate obstipation and greatly distended abdomen was underdeveloped physically and mentally. Operative interference was taken into consideration. Striking improvement was derived with thyroid gland therapy, 20 mg. Pulv. gland. thyreoid. sicc. twice daily, and among other things a regular stool passage was obtained. Deutsch is of the opinion that the thyroid gland hormone directly assails the Auerbach plexus and hence the tonus of the wall muscles of the intestine. Biedl observed an increase in intestinal peristalsis after injection of thyroid gland extract. A direct influence of the thyroid gland on the parasympathetic and sympathetic nervous system is indeed quite evident, yet positive proof of this is lacking. Cori points out that the tests of the vegetative nervous system is changed after injection of thyroid gland extract. Falta also confirms this.

The Treatment of a Case of Bulbo-Spinal Myasthenia with Extract of the Tuber Cinereum. — M. C. L. Urechia. (*Bull. et mem. Soc. méd. hôp. Paris*, **45** : 784, 1929.)

The author holds it is illogical to administer total extract for the investigation of cerebral organotherapy and thereupon recalls that the total extract of the anterior lobe as well as that of the posterior lobe is to be differentiated. In one case with classical symptoms of bulbo-spinal myasthenia a noteworthy improvement was achieved by means of treatment with an extract of the tuber cinereum.

Discussion on the Severe Hemorrhages following Parturition. — Voron. (*Bull. Soc. d'obstét. et gynécol.*, **18** : 357, 1929.)

In hemorrhages following puerperal infection the author unrestrictedly rejects curettage and recommends, instead, the administration of medicinal therapy, for example ergotin or pituitary extract. The medicinal therapy will next be tested in cases where the hemorrhage is caused by retention of the placenta.

Thyrotoxic Myocarditis. — J. Strickland Goodall, and Lambert Rogers. (*Brit. Med. J.*, No. 3468 : 1141, June 25, 1927.)

Most slowly acting poisons which affect the myocardium decrease its tone and usually raise its irritability as well. In thyrotoxicosis the first symptom is usually tachycardia, at first intermittent, then continuous, followed in the later stages by cardiac irregularity, myocardial exhaustion, and even sudden death.

In the later stages of mild cases of thyrotoxicosis, or in the early stages of very acute ones, the heart may become irregular owing to auricular fibrillation and then the normal co-ordinate contraction of the auricular muscle fibers does not occur; the different bands of auricular muscle contract irregularly and more or less independently. The degree to which this dissociation and inco-ordination has occurred determines whether the resulting fibrillation is of the so-called coarse or fine variety. Generally speaking, the condition develops after the disease has been in progress for some years, and must be regarded as indicating that the myocardium is profoundly

(*Concluded on page 251*)

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poisoned or that degeneration has definitely commenced. Occasionally Graves' disease starts with auricular fibrillation, and in these cases the condition usually persists. Not infrequently (about 5 per cent) auricular fibrillation develops during or soon after operation on the thyroid, and may occur after any operation, from simple ligation to extirpations of varying extent. Usually the condition is only temporary. Its onset is often synchronous with a rise in blood pressure. On the other hand, cases of Graves's disease which show auricular fibrillation, which may in some cases have persisted for years, are frequently cured of the fibrillation after removal of the greater part of the thyroid, especially if they are treated by quinidine, which appears to influence materially many of these cases after partial thyroidectomy. The cure of fibrillation by removal of the thyroid is a recognized treatment.

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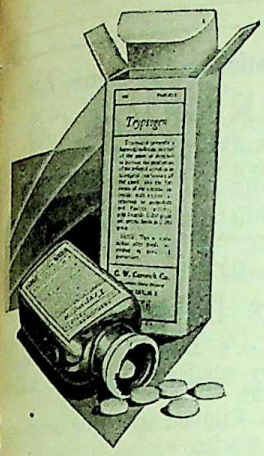
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OUR organotherapeutic products are made from fresh glands of healthy food animals, in our own laboratory, under the supervision of competent chemists. All moisture has been removed from these gland products and they will keep indefinitely if contents are not exposed to moisture and bottle is kept tightly corked.

The manufacture of gland extracts is not a side line with us, but is our only specialty, our only business. We stand or fall on their quality and potency.

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Diabetes mellitus; glycosuria and defective carbohydrate metabolism. Also useful in certain pancreatic disorders, and as an adjunct in hypertension.

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Trypsogen may now be obtained in enteric coated tablets which pass through the stomach unchanged and dissolve in the intestine, ready for immediate absorption. Same sizes as Trypsogen.

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Tablets: A homostimulative extract from the duodenum.

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THE ECONOMIC ASPECT OF DIABETIC TREATMENT

The diabetic in moderate circumstances with only slightly reduced carbohydrate tolerance---mild diabetes---presents a different problem from the well to do patient who can afford leisure and the luxury of constant medical attention with laboratory control.

The poor patient must continue at his work.

His diet must be adjusted to the energy expenditure of his work and he must receive routine treatment designed to increase his glucose tolerance and gradually effect a regeneration of the defective pancreas.

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Vol. XIV JULY-AUGUST, 1930 No. 4

The Journal of Organotherapy

A Record of Progress in the Study of the Internal Secretions and Metabolism

G. W CARNRICK CO., *Publishers*



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The treatment of amenorrhea by drug therapy is ineffective. Only in the body itself are those peculiar compounds synthesized which furnish the stimulus to menstruation. Hormotone is an active, potent combination of the hormones which act together in initiating and controlling the menstrual process.

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What Trypsogen Is

Trypsogen is manufactured from pancreas substance by a process which retains certain internal secretions controlling the oxidation of sugar and the storage of glycogen in the liver. In addition it contains the enzymes of the pancreas which are necessary to correct the associated defects of faulty digestion and absorption. The process of manufacture insures the retention of activity of both internal secretion elements and enzymes. By precise experimental methods it has been shown that these elements are absorbed from the intestinal tract and favorably influence the diabetic process.

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What Trypsogen Does

TRYPSOGEN
Aids in the Utilization of Sugar.
Aids in Storage of Glycogen in the Liver.
Depresses a Relative Adrenal Hyperfunction.
Improves the Associated Defects of Digestion and Absorption.

Trypsogen not only exercises a direct action on the disturbed carbohydrate metabolism through the absorption of the internal secretion principles, but also exercises a slower effect in stimulating the regeneration of the diseased insular tissue of the pancreas. The active principles obtained from the pancreas exert a greater effect on the abnormal carbohydrate metabolism of diabetes than any known substance.



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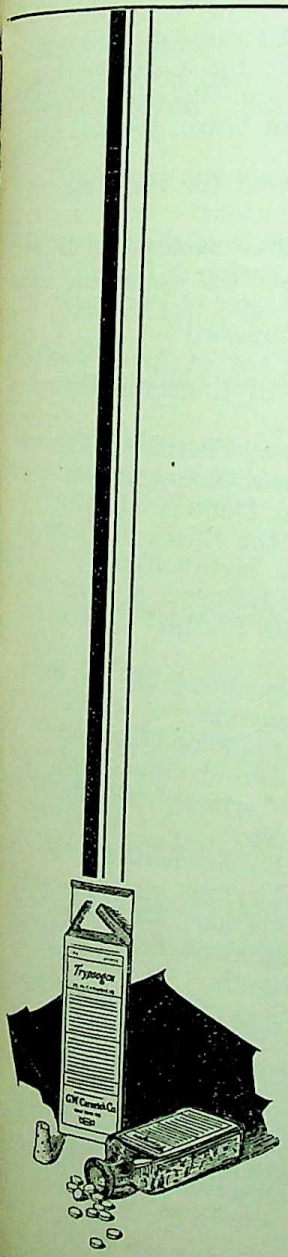
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THE ACTIVE PRINCIPLES OF THE PANCREAS



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What Authorities Say

¶ Pancreas preparations administered through the intestine "can be absorbed and can function to cause the utilization of sugar". (J. R. Murlin, *Endocrinology*, May, 1924, p. 339.)

¶ "The presence of something derived from the pancreas, either its digestive ferments or some internal secretion besides insulin, is necessary for the maintenance of normal metabolism." (Charkoff, Macleod and Markowitz, *Journal of Biological Chemistry*, 63, p. LXXI, February, 1925.)

¶ In reporting ten carefully controlled experiments with various pancreas preparations orally administered, Prof. P. J. Cammidge says of Trypsogen---"Would seem to contain an antiglycogenolytic fraction which is absorbed from the alimentary tract". (*British Medical Journal*, Dec. 26, 1925.)

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(W. P. Graves, M. D., Professor of Gynecology, Harvard Medical School.)

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Rejuvenation and Stimulation of Sexual Activity

REJUVENATION and restoration of sexual function are not synonymous. Nothing can prevent the structural changes of age. Special functions, however, may be increased by endocrine therapy.

THERE is a very sharp difference between rejuvenation and mere stimulation of sexual activity. Rejuvenation implies a complete restoration to a condition of youth, not only the feelings and functional capacity but the entire actual and potential possibilities of the organism. Frequently, however, the word rejuvenation connotes something entirely different — the restoration of the sexual capacity. This use of the word has become particularly prevalent in connection with gland transplantation operations, rejuvenature of the vas, etc.

So far as therapeutic efforts at rejuvenation are concerned, they are hopeless from the beginning. No method or drug has ever been found which will stay the slow gradual tissue changes characteristic of the age process. These changes are inevitable. Professor A. S. Warthin states that they can not be regarded as disease, rather the whole process is a physiological entity and the result of involution processes inherent in the organism. The "major involution" is the aging process of the organism as a whole. Aging of individual organs is a "minor involution." The changes which affect the tissues of the body as a result of the age process are not simple, but, in general, active functioning tissue of all types is replaced by connective

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tissue. This slow process of involution proceeds throughout life and in later periods the structural alterations utterly preclude re-establishment of function at the levels of early life.

Rejuvenation must be considered from a dual standpoint — the exciting or therapeutic agent causing the rejuvenation and the reacting organism to be rejuvenated. Hygienic measures in general are rejuvenation measures, but the connotation of the term rejuvenation to both laity and profession refers to sexual rejuvenation so that the current concept has entirely lost the full significance of the term.

In the case of therapeutic attempts at "rejuvenation" with the sex glands, it may be remembered that they exert not only a sex specific influence on the reproductive system, but a general influence in increasing metabolism and tonicity of the somatic tissues as well. As a result of gland transplantation experiments and ingestion of sex gland preparations it has been possible to show beyond all doubt that the functional activity of the sexual system may be heightened and the general vigor of the body increased. Voronoff and others have given striking evidence of this kind. Steinach, by an entirely different method, succeeded in increasing the interstitial hormone production and achieved the remarkable results now well known to the world.

Very recently highly concentrated preparations of the active male sex hormone have been prepared by Gallagher and Koch (1) and by Funk, Harrow and Lejwa (2). In 1928 McGee, Juhn and Domm (3) published the results of their researches on the activity of extracts of bull testes, using the secondary sex characters of capons as a means of measuring the activity. Making use of the methods developed by Allen and Doisy, Frank and Gustavson and others, for extracting the estrous hormone from follicular liquid, placenta, etc., they showed that lipoids exhibiting the property of stimulating the growth of the comb, wattles and ear lobes of the capon can be extracted from bull testicles. Briefly summarized, they showed:

"1. A benzene soluble lipin fraction obtained from bulls' testicles when injected into brown leghorn capons causes growth of the comb, wattles and ear lobes.

"2. The amount of lipin material injected daily represents from 150 to 500 grams fresh testicle tissue.

"3. Although the reactivity of individual capons varies, these variations are of such a nature that this biological reaction can be used as a rough quantitative method for assaying such lipin preparations.

"4. Very frequently serious local reactions appear at the site of injection and much unabsorbed material may remain.

"5. When injected into bilaterally castrated hens good comb growth was induced.

"6. The crude lipin found in the benzene soluble fraction can be freed somewhat from non-potent material by fractional precipitation by methyl alcohol, ethyl alcohol and acetone or by extraction by liquid ammonia.

"7. Nine hours' boiling of the active material with alcoholic sodium hydroxide still leaves considerable potency in the non-saponifiable fraction.

"8. The activity was lost completely after boiling with alcoholic sodium hydroxide for eighteen hours."

Using as a test method spermatomobility tests which depend upon extending the life of the spermatozoon in the isolated epididymis, Moore and McGee (4) proved that these extracts are also effective in mammals (guinea pigs). Funk, Harrow and Lejwa obtained their most potent male hormone preparations from the urine of young men although the testicle extracts also gave definite results. They were led to make use of this source for the hormone by the finding of the hormone in the blood of male cocks by Pezard.

"It seems logical to conclude that since the male hormone is in the blood it would probably also be found in the urine."

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Frank and his associates had also shown the presence of the female sex hormone in the urine.

Funk, Harrow and Lejwa give some interesting though inconclusive data on the relationship of the male and female hormone in capons. "It does seem, however, as if in well castrated animals the male and female hormone may act antagonistically, at least in so far as secondary sex characters are concerned."

Some of the chemical characteristics of the male and female hormone are very similar. "It was now shown that what is true of the female hormone is true of the male hormone: both form alkali salts which are largely soluble in ether."

The specificity of the substance extracted from the testes was determined by Gallagher (5). Extracts of brain, ovary, pancreas, prostate, thyroid, suprarenal, kidney, liver and seminal vesicles failed to give any activity when prepared by the method used in obtaining active extracts from the testes.

In considering the sex hormones, the highly important hormone of the anterior pituitary must also be included. Evans (6) and Evans and Simpson (7) have clearly shown the presence of this hormone.

"Two hormones are secreted by the pars anterior of the mammalian hypophysis, one required for normal growth and the other for normal development of the gonads, thyroid and suprarenal cortex. As regards its effect on the sexual system, the second hormone can be completely nullified by simultaneous administration of the first — the growth substance. Evidently nature has provided the necessary nice adjustment in the relative amounts of the two substances secreted. That the growth of the animal is usually accomplished before the attainment of sexual maturity may therefore plausibly be due solely to the early predominance of the growth hormone."

The sex hormone of the anterior pituitary may be recovered from the urine and is active in both male and female. In further work on the male testicular hormone, if urine is used as a source, the hormone of the anterior pituitary will have to be carefully excluded.

But all of these results, striking as they are, must be surveyed critically and the limitation of this or any method of "rejuvenation" clearly recognized.

It is entirely possible to stimulate the deficient physiological mechanism (including the sexual) to greater temporary activity. Under competent medical supervision such results are frequently desirable but there are dangers and the stimulation, therefore, should not be too great for the structurally weakened organism. The limitations of this type of therapy are well given by Peritz (8).

"If one takes note of this rejuvenation, one must say even in the case of the animal, that not a total but only a partial rejuvenation occurs. Only in quite fixed domains is the function increased. In the human being it asserts itself more strongly. Man lives under altogether different conditions in the struggle for existence, from the animal, and is, accordingly, exposed to altogether different dangers; which above all things involve also the nervous system, and the nerves which regulate the various internal organs, in particular the heart. Moreover, man, because of the finer manner of reaction of his nervous system also uses stimulants, such as coffee, nicotin, alcohol. The injuries which are effected by these stimulants have nothing to do with old age, can consequently also not be set aside by a rejuvenation. On the contrary, it is even to be feared that individuals in whom the heart or circulatory system has suffered, will be injured by the rejuvenation, since now the renewed energy and joy of living will overwork the already diseased tissue still more and thus lead to a more speedy exhaustion of it.

"One must also not imagine that possibly through a rejuvenation the intellect will be increased, since if one wishes to think in rough organic terms, the intellect is dependent upon

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the number of ganglion cells, the communication of these ganglion cells among themselves and the physicochemical processes in them. The sex gland hormone has, so far as known up to the present, only a stimulating action and the task of hastening the course of psychic processes. There will, accordingly, be no improvement if the sex gland hormones light on an old brain, since a part of the ganglion cells is destroyed and this abolition of function can not be set aside.

"Nothing is as yet known concerning a prolongation of life through transplantation of the sex glands. If one desired to demonstrate this in the animal it would be necessary to observe many generations of animals, and moreover, a great number of control animals in which no rejuvenation had been undertaken and just as great a number of animals which had been rejuvenated. Both groups would have to be of the same origin and under similar conditions. The time which has elapsed since the application of this method is much too short to allow of a decision concerning the animals.

"In man the situation is much more unfavorable. The transplantation has been undertaken only in isolated individuals. Their constitution is not known, the lesions are also not known which disease and struggle for existence have inflicted on their constitution. How can one tell whether their lives have been prolonged! It is, however, probable that a prolongation of life has not occurred through it, since death from old age rests on the fact that the hereditary substance which the individual cells of individual organs have received, is gradually consumed. The product furnished by the sex glands, however, merely represents a stimulant and not a substitute for destroyed and consumed cellular elements."

A true rejuvenation is impossible under the conception of a slow structural metaplasia of one tissue to another. Youth could only be maintained by preventing those unknown factors in the vital processes which slowly change the character of the tissues themselves. Many of the functions of the body are controlled wholly or in part by the several hormones; particularly is this true of the purely vegetative, vital processes. In the age process, however, the endocrine tissues themselves are subject to the retrograde changes which result in progressive functional inefficiency.

In the testes old age gives rise to smaller testes, a result of atrophy of active secreting tissue or of fibrosis. The spermatogenic cells as a rule are the first to be affected and the interstitial tissue outlasts it. In old age, therefore, sex desire (persisting as an established psychic reaction) and sexual ability may persist long after the production of spermatozoa has ceased.

In its broader sense rejuvenation depends not only on the hormones of the sex glands but also, as pointed out by Leschke and others, on several of the glands of internal secretion. Particularly important are the pituitary (anterior) and the thyroid. Again certain substances (vitamins) taken in the food are necessary. Evans and Bishop (S have shown that a diet sufficing to maintain animals in perfect health may still leave them sterile and incapable of reproduction. The vitamin is apparently a special one and not identifiable as one of the known vitamins necessary for other physiological functions.

So far as sexual ability is concerned however, the influence of diet and vitamins is doubtless not important. The vitamin of Evans and the diets described by Macomber in connection with fertility are important however, in the maintenance of the fertility characteristic of young animals and therefore should be considered in rejuvenation.

Rejuvenation in its broader aspects is impossible. Hygienic measures, moderation in food, alcohol, tobacco, exercise and stimulants, the use of endocrine products (plus glandular) and proper diet all contribute to the maintenance of a youthful mind and body with the later decades of life.

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The direct increase of activity of the sexual system may be successfully attempted with those hormones which normally control their functions. There can no longer be any doubt that several hormones are necessary. Certainly the active sexual hormone of the testis and anterior pituitary are required. Thyroid would appear to be valuable even though a specific sex effect has not been shown. Thyroid maintains a normal metabolic rate and gives added energy output, necessary in any effort to restore general body efficiency. These substances may all be given orally. It is interesting to note that Funk, Harrow and Lejwa found that "It would seem, from the results here recorded, that the activity of the male hormone does not entirely disappear when given by mouth. It also appears that testicular extracts, like urine extracts, are active although the comparative activities of these two extracts have yet to be determined." With a proper and potent preparation of this type, rejuvenation of the sexual function is possible. It is not, however, a therapy to be uncritically applied: certainly the laity should not attempt self-medication. Careful medical attention is necessary to determine whether a case is suitable for treatment and to prevent accidents from arising in those in which the general physical condition may be sufficiently below par to undergo excessive functional activity of a particular physiological mechanism.

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Clinical Observations concerning Respiratory Basal Metabolism

(Translated from the article by Prof. F. de Quervain and Dr. F. Pedotti, First Assistant Physician at the Surgical Clinic, Berne.)

(*Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 39 : 646, 1926.)

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After the importance of the thyroid gland for the metabolism of gases, and thereby for the respiratory basal metabolism, had been demonstrated by means of physiological experiment and numerous clinical observations, we were concerned with the problem of investigating, in one class of Basedow patients, in material consisting of

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common goiter bearers and cretins, in order to determine what relationship exists between the clinical estimation of thyroid gland function and the basal metabolism.

Further attempts were made to determine, within the limits of our observational material, what other pathological conditions, not primarily connected with the thyroid gland function, would likewise influence basal metabolism.

An additional problem was that of tracing the relationship between basal metabolism, respiratory quotient, pulse frequency and volume per minute of breath. The point was mainly, to determine whether this relationship — at least in the case of disturbances of thyroid gland function — would permit the estimation of the basal metabolism without the circuitous method of the determination of the consumption of oxygen.

Finally it remained for us to test the relationship (investigated in an earlier work by Dr. Pedotti and Dr. Branovacky) between basal metabolism and deficiency in the Asher-Streuli rat experiments from goiter bearers of various kinds, on a somewhat larger material.

Since we see in the gas metabolism method the first, and up to the present the sole possibility of determining numerically the function of the thyroid gland, or at least *one* component of it, we were concerned with obtaining not merely approximate values. We did not content ourselves with the simple determination of absorbed oxygen, but used a carefully constructed Tissot apparatus, according to our reports, obtained from the Stoppani Company, which had carefully counterbalanced bell weight and water valves sealed with liquid paraffin, and which proved very satisfactory. The air of respiration was submitted to a total gas analysis and in the majority of cases three analyses were made for each experiment.

The calculation of metabolism under 17 years was based on the standard values of Benedict, for adults on those of du Bois, using the formulae and tabular material worked out by Boothby and Sandiford in the Mayo Clinic (1). The experimental procedure was briefly as follows:

On the evening before, between 6 and 7 o'clock, a light meal, on the day of the experiment, an empty stomach, with avoidance of bodily exertion and much walking. (Patients not residing at the clinic must be brought to the laboratory in a conveyance.)

First, comfortable resting in bed, undressed except for underclothing, until pulse and breathing had become entirely regular. Then preliminary experiment with controls of pulse and breathing and calculation of the volume per minute. Then the main experiment. If the volumes per minute of both determinations varied greatly, the experiment was not valid and had to be done over. It is important that with timid patients, the experimental room should not cause excitement. For this reason we cut off the patient's view of the apparatus with a curtain. The personnel must understand that they are to work silently through the entire procedure. The importance of absolute muscular quiescence has been demonstrated again in the latest control experiments of Benedict. If there is failure on this score the entire accuracy of the gas analysis is not valid.

In the following a series of 178 cases will be reported, of which 42 cases were hyperthyroid, 52 cases had common goiter and 4 cases cretinism with and without goiter. There are 34 cases of various illnesses, in which the thyroid gland is not ostensibly particularly associated. The percentage of

1. In a recent communication (1925) Benedict draws attention to the fact that the American standard values for women are about 5 per cent too high. Nevertheless, since our Swiss values agree fairly well, it shows above all, that the B.M. determination in individuals who are not trained to the method by a large number of tests, as a rule, results in values a little too high, because it is almost impossible to induce absolute muscular quiescence in patients. This error is practically constant in all our determinations of gas metabolism; having heeded all known precautions, however, this amounts to only a few per cent.

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individual goiter forms does not agree with that of our clinically observed material for the reason that gas metabolism experiments were done on only a part of the goiter individuals without clinical disturbance of function and because a good portion of the cretins were not successful for the experiments by reason of their mental deficiency.

From the investigation it was concluded, particularly in those cases where there was tracheal stenosis, that quiet regular breathing was impossible for the calculation of the basal metabolism.

We shall now report the results in accordance with the various viewpoints mentioned above.

I. Basal Metabolism and Clinical Findings

1. Average Values of the Individual Groups

We begin by assembling the average values of the individual groups and by investigating what causes the important deviations from the group median in individual cases. We note that the connection of the isolated cases to the functional groups had been assumed exclusively on the basis of *clinical* symptoms and *not* on the basis of gas metabolism experiments, for it was a problem of testing the importance of the latter for the functional analysis.

Table 1. Survey Table concerning the Composition and the Average Values of the Groups

Groups	Pulse frequency	Volume per minute	R. Q.	Basal metabolism in %	No. of cases
1. Basedow goiter before treatment	109	7.6	0.73	+35.9	42
2. Common goiter	80	5.7	0.78	−0.6	52
3. Cretinism with goiter	68	6.0	0.83	−8.0	32
4. Cretinism without goiter	78	4.7	0.84	−11.4	9
5. Operated Basedow and other goiters (excl. the control experiments from Groups 1-3)	71	5.2	0.75	−7.5	9
6. Diverse cases	77	5.8	0.76	+2.4	34
				Total	178
				Control experiments	68
				Total number of experiments	246

From the above survey table it is evident that the group of cases clinically designated as *hyperthyroid*, on the average, show the highest pulse rate, the highest volume per minute and, with +35.9 per cent, the highest basal metabolism and yet the lowest respiratory quotient.

The instances with no clinically recognized disturbance of function, that is *euthyroid goiter*, show normal median values all along the line, with a basal metabolism of −0.6 per cent.

Goiter associated with symptoms of *cretinism* (including the border cases) shows an average basal metabolism of about −8 per cent, with normal volume of breath, slow pulse and a respiratory quotient higher than that of the above mentioned group, *i. e.* 0.83.

Cretins without goiter show a still lower basal metabolism: −11.4 per cent with minimal volume of breath and a respiratory quotient somewhat higher than the foregoing groups, namely 0.84.

The *group of diverse cases*, which require special mention, show an average metabolism of +2.4 per cent, with pulse frequency, volume of breath and respiratory quotient functioning in normal values.

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The values obtained for the first four groups show in the arithmetical mean, an important gradation from Basedow goiter down to cretins without goiter. The relationship between the clinical picture and the gas metabolism will be still more striking if one considers the graphic table and thereby the distribution.

Table 2. Clinical Thyroid Gland Function and Basal Metabolism. All Thyroid Gland Cases (As in All the following Tables excepting Tables 3 and 11)

0

Groups	− 30-39	− 20-29	− 10-19	− 0-9	+ 0-9	+ 10-19	+ 20-29	+ 30-39	+ 40-49	+ 50-59	+ 60-69	+ 70-79	+ 80-89	+ 90-x Basal metabolism %
Basedow goiter (hyperthyroidism)					· · ·	· · · · · · · · · · · · · · ·	· · · · · · · · · · · · · · ·	· · · · · · · · · ·	· · · · · · · · · ·	· · ·	·	· ·	· ·	·
Goiter without functional disturbance (euthyroidism)			· · · · · · · · · · · · · · ·

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results confirm the facts already known, so that it is superfluous to linger over them. The rather low basal metabolic rates, even in cases of severe Basedow, in agreement with numerous reports in the literature, rest in part on the careful consideration and avoidance of all those things which can increase the metabolism. Elimination of masks, least possible disturbance, ample tube connections, easily functioning valves, careful counterbalancing of the spirometer bell are factors of importance which intelligent patients will soon recognize if they have once been tested with a poorly functioning apparatus.

Only three cases in which the gas metabolism lay in the realm of normality, *i. e.* under ±10 per cent, deserve mention.

1. Z. E., 28 years old, female. Possessed a nodular goiter for years, for the previous month slight basedowification, *i. e.* appearance of heart palpitation, insomnia, tremor, exophthalmos, B. M.+9.4 per cent. Histological: Struma nodosa parenchymatosa microfollicularis.

2. R. N., 36 years old, female. Treated for 5 years for slight Basedow. Slightly diffuse and nodular struma. Acceleration of pulse, some tremor, no exophthalmos. Diagnosis questionable, nevertheless, "forme fruste." B. M.+7.5 per cent. Histological: Struma nodosa parenchymatosa.

3. St. M., 30 years old, female. Nervousness. Treated for two years as a slight Basedow case. Still in a quiescent phase. No definite clinical aspect. B. M.+4.6 per cent. Histological: Slightly diffuse Basedow changes.

In all three cases the Basedow symptoms were so slight that the diagnosis seemed questionable, and a low basal metabolism was to be expected.

3. The Common Goiter

The Goiter without Functional Disturbance of the Thyroid Gland

The cases in this category oscillate so closely around the null line that their average value of −0.6 practically is equal to 0 per cent. Only seven cases overstep the ±10 per cent limit, some above and some below, with limiting values of −14 per cent and +15 per cent. Pulse, volume per minute and respiratory quotient congregate, however, around the average value, with a fairly slight distribution. The three values combine in such a variable manner in an individual that it is impossible to draw any conclusion as to the basal metabolism from one of them, or from pulse and volume per minute combined.

Concerning the significance of the ±10 per cent excessive values, the following may be said:

Values from −11 to −15 per cent were found six times. In none of these cases was there any clinical sign of under-functioning of the thyroid gland or any stigmata of cretinism. From a purely *clinical* standpoint, the matter does not concern the border cases of the latter. Besides, a short preliminary control experiment twice gave normal values, namely −1.3 per cent instead of −11 per cent and −10 per cent instead of −15 per cent. Histologically, in the five operated cases, various types of goiter were found, alone and in combination: Struma colloides diffusa, colloides nodosa, parenchymatosa nodosa. Either we must agree that in these patients a clinically latent, relatively temporary underfunctioning occurred, or we must, with Benedict himself, incidentally, extend the limits of the "normal" under the ±10 per cent.

Twice, values of more than +10 per cent were found, namely once, 13 per cent and once, 20 per cent. In both cases dyspnea occurred, in the one case (+20 per cent) nervousness also without any other Basedow symptom. We must abandon the attempt to determine whether the high value for the basal metabolism is traceable to the dyspnea or whether one must account it as a casual occurrence. The latter assumption is more acceptable for the +13 per cent than for the value of +20 per cent.

One point must be emphasized, namely

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that the histological condition of the goiter appears to play no part in these deviations from the average. After the rat experiments we must agree that the colloid strumæ are as active as the parenchymatous small follicular strumæ. This is also recognizable in the investigation of the thyroid gland venous blood, which proves no more active than the blood of the general circulation. Therefore, the question may be posed whether the high basal metabolic values in ordinary strumæ chiefly affect colloid strumæ. We find in 15 cases of genuine colloid strumæ an average value of +0.6 per cent, such an insignificant difference as compared with the median of the group that we have to negative this question *for our material*. This does not exclude the fact that, in other regions with greater Basedow frequency (for example Norway, and according to Holst), colloid goiter can not give higher values. The same applies to the border cases of Basedow (Basedow distribution according to Hellwig, Breitner, latent thyrotoxicosis according to Holst). We must hence straightway assume a varied activity for colloid struma with regard to the geographic distribution.

4. Cretinism with Goiter

Here, for the first time, the differentiation between the gas metabolism investigations on cretins with goiter and the investigations on cretins without goiter is encountered (2). While the disease picture in cretins with atrophic thyroid glands, *without* goiter, is so typical that there can be no doubt as to its identity, the state of affairs is different with cretins *with* goiter. We find here an indefinite transition from euthyroid goiter bearers to cretins with goiter, and it is often only a matter of opinion whether one wishes to accept a certain degree of dullness, an unobtrusive lack of intelligence, slight speech defect, a little deafness as a slight degree of cretinism or not. The principle diagnosis is so simple that we observe these constitutions progressing towards the other side, without sharply defined borders, to the worst forms of cretinism in which the diagnosis is not at all intricate. That the border cases trending towards euthyroidism show a normal gas metabolism is not to be wondered at if we assume the extended limits which must be recognized as "normal." Let us look at the following clinical cases of cretinism with plus values:

1. B. C., 14 years, male cretin. Conglomerate goiter, with difficulty in breathing. Very moderate intelligence. Suggesting hypothyroid constitution, without pronounced stigmata. B. M. +1.3 per cent. Histological: Struma nodosa parenchymatosa microfollicularis.

2. B. M., 14 years, female, moderate intelligence. Underdeveloped bodily. Cretinoid constitution. B. M. +1.0 per cent. Histological: Struma nodosa colloides.

3. D. M., 24 years, female. Nodular goiter with dyspnea. Nervous, excited, yet apparently cretinoid. B. M. +3.6 per cent. Histological: Struma nodosa colloides.

4. H. Chr., 27 years, male, deaf, cretinoid constitution. B. M. +7 per cent. Histological: Struma nodosa parenchymatosa et cystica.

5. L. E., 42 years, female. Rapidly developing nodular goiter, left. Right, atrophic thyroid gland. Slight difficulty in breathing. Pronounced cretinoid constitution. 140 cm. high. Little intelligence. B. M. +1.6 per cent (−9.6 per cent post op.). Histological: Proliferating struma according to Langhans.

6. E. A., 64 years, female. Nodule conglomerate. Dyspnea. Total cretin. 147 cm. high. B. M. +13.17 per cent. Histological: Struma nodosa colloides partim cretacea.

7. B. E., 46 years, female. Deaf and dumb cretin with constricting goiter. B. M. +6.5 per cent. Could not be brought to quiet breathing.

The first four cases are cretins of less severe degrees, still capable of being educated. Dyspnea was twice observed, once excitability, both factors capable of increasing the

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B. M. In the fifth case there was a badly degenerated nodular goiter, after its removal the B. M. dropped to −9.6 per cent. The sixth and seventh cases concern total cretins with the expected impossibility of obtaining complete quiescence for the investigation. If we say that *Degree of Cretinism I* = slight and *Degree of Cretinism III* = worst, in connection with the *metabolism* of goiter-bearing cretins, the accompanying table is the result.

Table 3. Degree of Cretinism and Basal Metabolism

Degree of cretinism	− 30-39	− 20-29	− 10-19	− 0-9	0	+ 0-9	+ 10-19	+ 20-29
I. (23 cases)	·	·	· · · · · · · · ·	· · · · · · · ·		· · · ·		Basal metabolism %
II. (5 cases)	· ·			· ·		·		
III. (3 cases)				·		·	·	

From this table it is evident that with cases easy to experiment on, hence the greater number of cases (about ¾) forming our statistics on cretins of the first degree, we find all gradations of gas metabolism from +9 to −39, yet in *ca.* 5/6 of the cases there are values under 0, *i. e.* under the normal average. The gas metabolism in this degree of cretinism is generally depressed, yet additional insignificant circumstances can bring it, at least transiently, to the normal height. The gas metabolism experiment appears to be less a criterium in these border cases than the general clinical observation. The more severe the cretinism, the smaller the proportion of cases accessible for metabolic investigation. From our cases of Degree III most must be eliminated from the experiment. In the three cases represented in the table the experiment could be done only with great difficulty.

(*To be continued*)

Practical Therapeutics

Pancreas Enzymes in Local Treatment

ADVANTAGE may be taken of the action of the proteolytic enzyme trypsin as a local application. Its capacity to digest the protein of dead tissues is extraordinary and inasmuch as little use has been made of pancreatin in medicine, even as an agent in digestive disturbances, physicians generally are not fully appreciative of the powerful character of its action. In the manufacture of pancreatin in the G. W. Carnrick Co. factory workers frequently develop bleeding from the fingers, palms of the hand, the nose, etc., and examination of these sites discloses that the light pancreatin powder settling on the moist surfaces has digested all

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dead epidermis and leaves the living dermis exposed. The U. S. Pharmacopoeia prescribes no standard for strength of trypsin in pancreatin; it fixes only the amylolytic activity. There is, therefore, some variation in the trypsin activity of commercial pancreatins, and salves or ointments made up containing pancreatin for local application should be used cautiously until the strength has been determined.

Uses of this kind — furuncle, acne vulgaris, eczema seborrhoicum, cicatrices, indolent indurated ulcer edges, etc., are described in the abstracts of articles by Axmann, Kuhn and Bassmann (below). Such pastes, in view of their definite activity, under careful supervision, should find a useful place in practice.

Concerning Cosmetic Treatment of Cicatrices with Pancreas Salve. — Axmann. (*Med. Klin.*, **24**: 67, 1928.)

Cicatricial distortions following surgical wounds often spoil the otherwise good results, to say nothing of the cords of the cheloids as thick as a finger as they are occasionally to be seen in severe, healed, old lupus foci. And yet here this may be quite satisfactorily prevented if one proceeds with necessary perseverance. Following a preliminary treatment with poultices of pepsin-hydrochloric acid for the purpose of softening, the cicatricial tissue is vigorously rubbed in with pancreas salve and massaged with the adjuvant of electrical vibrations. There may possibly be a too great skin irritation following this treatment, and this may again be equalized by boracic ointment or powder. Through this simple procedure, carried out for months with great perseverance, extensive cicatricial fields in addition to cicatricial cords almost as thick as a finger, especially on the face and extremities where they frequently impede movement, are brought to the vanishing point (the patient may himself accomplish the treatment). The pancreas salve appears to develop an especially profound effect, which as is self-evident, appears also of importance for suppurating wound surfaces.

Concerning Treatment with Pancreas Enzymes. — Kuhn. (*Münch. med. Wochenschr.*, **75**: 289, 1928.)

The great advantage of enzyme ointment and of enzyme powder lies in the fact that they do not attack or irritate the healthy tissue in any way. They merely liquefy the necrotic tissue and digest pathologic products of the skin and mucosa. The excellent results which the author has obtained for years with pancreas enzyme preparations, are shown in the following diseases:

(1) Suppurative wounds. In particular wounds which arise through cauterization with chemically impure acids in the metal industry and show a poor healing tendency in general, heal up smoothly within a few days under enzyme ointment dressing. Suppurated insect bites also, which show a solid scab following opening of the pustule, which was not to be influenced either by bathing or indifferent ointments, were healed in a very short time by pancreas enzyme.

(2) Furuncles, which were treated with enzyme ointment, healed so well that the author considered incision therapy as superfluous.

(3) Acne vulgaris. The pustules dried up very soon. Anointing of the face before retiring, without bandage, sufficed for the patient to be able to gently remove the scurf digested by the enzyme by washing on the next morning.

(4) Eczema seborrhoicum. The treatment takes longer, but the evening inunction also suffices in these cases and a light protective dressing in which the entire absence of irritation of the enzyme ointment against the healthy skin must be stressed as a great advantage.

(5) Rhinitis anterior. The adhering crusts are very easily softened by the ointment, so that they can be removed without pain.

Since the patient's ability to return to his work is hastened by the more rapid healing, the treatment with enzyme preparations is to be recommended in industrial practice.

Experiences with Roehm's Wound Ointment and Wound Dusting-Powder in the Treatment of Wounds. — Bassmann. (*Therap. Gegenw.*, **69**: 90, 1928.)

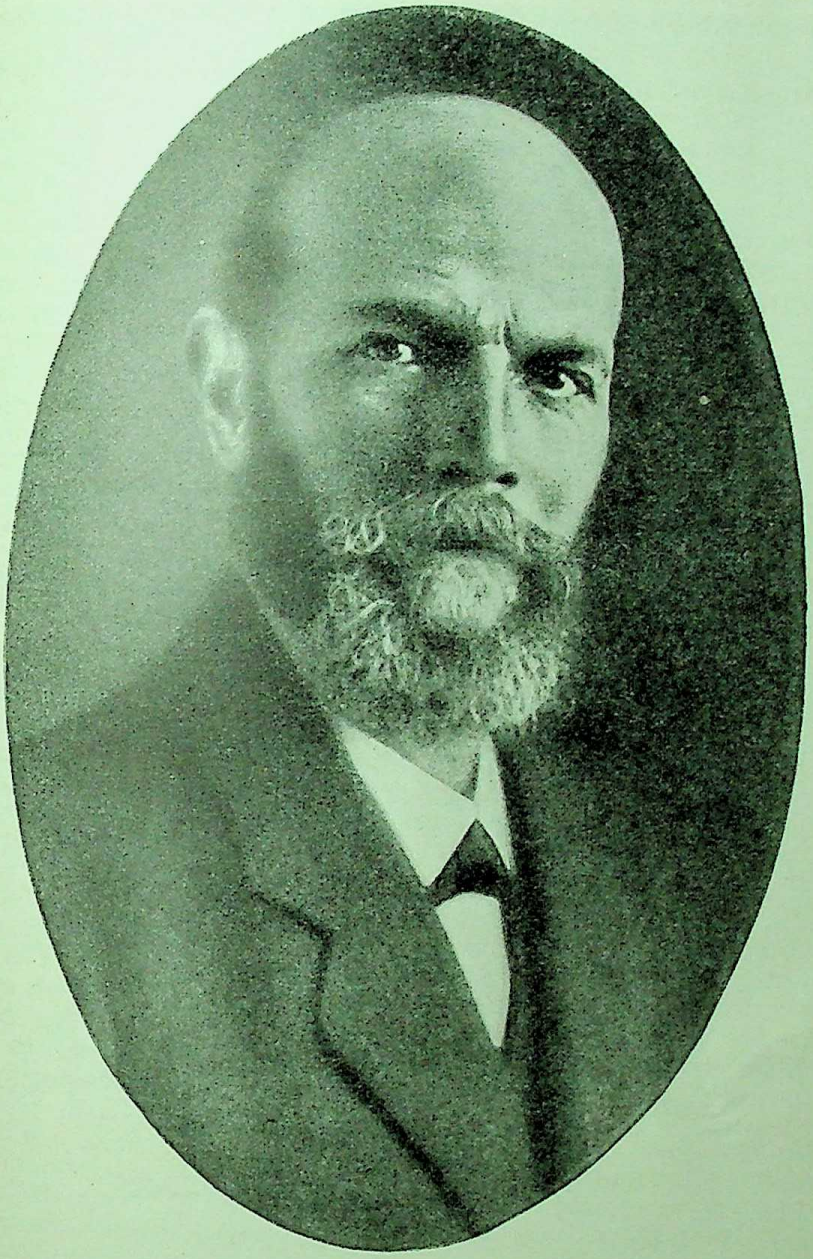
Roehm's wound dusting-powder and wound ointment consist of extract. pancreat., Zinc oxydat. and Vasel. flav. or Talc. venol. The most important ingredient is, to be sure, pancreat. extract, which owing to its ferment action, in particular that of trypsin, and also of the other constituents of pancreas secretion, aids the tissue in its work of cleansing wounds. Pancreas secretion through its

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The Doctor's Page



JOHANNES VON KRIES
(1853-1929)

To classify Johannes von Kries under the ption of one special line of endeavor is possible, for he is associated with contri- tions to physiology to physics in conjunc- with his physiological work and to psychology which appears to have developed out of these two studies. Mathematics, of course, formed the basis of these studies, and his bent for this subject was early displayed in "Principles of Calculus" published in 1886.

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This is still considered a classic and has a second edition published in 1927. Logic and philosophy have also received the attention of this unique individual. His interpretations and grasp of the thoughts of both Goethe and Kant are still the subject of much favorable comment.

Among German scientists von Kries is considered primarily a physiologist, for that was not only his life's work but also the subject in which he gave instruction for years. The rank of doctor rests both on his having qualified in the state examination (1874-1875), and on his excellent studies concerning the blood, the measurement of its flow, the activity of the heart and pulse, and particularly the work on the muscular and nervous systems.

Von Kries was born October 6, 1853, in the picturesquely fortified town of Graudenz on the Vistula River (now the Polish Grudziadz). His youth appears to have been a pleasant, unassuming period in which he was occupied with studies at the gymnasium at Marienwerder (1865-1869). His university studies were distributed between Halle, Leipzig and Zürich; he also attended the physiological institutions of Hermann von Helmholtz and Carl Ludwig, both of whom were inspirations and guides in his work at the laboratory, and in subsequent years. In 1880 he was installed as Professor of Physiology at the University of Freiburg. It was in this capacity that he laid the ground work for the "duplicity" theory of vision (rod and cone principles). In fact ophthalmology is much in debt to von Kries for the solutions of many intricate problems (for example, color blindness which he termed protanopia (red-blindness) and deuteranopia (green-blindness) and for instruments (such as Nagel's anomaloscope) without which this branch of science would be greatly impoverished. In 1881 he married, happily. (From this union there were four children; the oldest married the physiologist Nagel.) Besides the titular honors of *Hof-Rat* and *Geheimer-Rat* he had the distinction of being called to posts in Leipzig (1895), in Berlin (1897) and in Munich (1908).

Von Kries was fitted particularly to pursue the rôle he chose, for he had a faculty of interpreting the contributions of both predecessors and contemporaries, for conveying his interpretations in a clear manner and for carrying forward to still more complete results the intricate problems of such profound thinkers as, for example, von Helmholtz. Though the insidious malady from which von Kries suffered for years sometimes made the fulfillment of his tasks almost impossible, yet he never avoided even the smallest of his duties until absolutely forced. Only with the cessation of life (December 30, 1929) was von Kries released from the terrific combat between the desire to push forward his chosen work and the disease which was constantly undermining his powers.

Of his numerous works on physiology the most important is "General Sense Physiology." As early as 1891 von Kries contributed with a treatise "Concerning the Relationship between Physics and Physiology" in which he displays his ability in both subjects. A rectorate address in 1898 was entitled "Concerning Sense Perception," and there followed later (1901) an excellent study "Concerning the Material Basis of Consciousness." It is easy to observe how his thought processes actually were progressing away from pure physiology to its more abstract applications, namely psychology, and kept advancing until a culmination in 1916 with the magnificent work on "Logic." This, according to W. Trendelenburg, his pupil, was "a fountain of information" concerning the science of nature, of the mind and of some of the most important and most intricate problems of perception, presented by one whose keen mind "could well nigh push on to the very limits of knowledge."

In the realm of physics von Kries, like von Helmholtz, was interested in sound and presented in 1892 (*Zeitschr. Physiol.*) a treatise on "Absolute Sound," which added to his illustrious name still further honors. Carrying these principles further, in his characteristic way, he gave us a monograph entitled "What is Musical," which is considered the best essay on the physiology of music since that of Albert Billroth, with the same title. Furthering the studies of von Helmholtz concerning light, von Kries collaborated not only in editing but also in contributing in *Handbuch d. Physiol. Optik* (Handbook of Physiological Optics) especially with an article concerning the "Laws of Sight Perception of H. Helmholtz."

In yet another field of study did von Kries distinguish himself, namely that of Philosophy. The careful penetration of the

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Medical Subjects by Famous Masters



"THE DOCTOR'S VISIT," by Jacob Toorenvliet (1641-1719)
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Editorial Comment

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Menstruation, the Sex Hormone and the Renal Threshold

KNOWLEDGE of the menstrual process and of the female sex hormone has increased enormously in the past 10 years. Among those who have contributed the group at Mount Sinai Hospital, New York, headed by Robert T. Frank stands in the very front. Their contributions have been fundamental, original and scientifically sound. The demonstration of the active hormone in the blood and in the urine with the development of a technique for isolating it has been particularly enlightening. Very recently (1) Frank, in collaboration with one of his best known associates in this work, Morris A. Goldberger, has still further extended our knowledge of the relationship between the hormone in the blood and urine and the menstrual process and its abnormalities. Frank had previously shown that in normal women free from menstrual disturbance there is in the great majority of cases a definite increase in the concentration of the female sex hormone in the blood during the 10 day period just preceding menstruation. Just before or at the time of menstruation the hormone practically disappears from the blood and in non-pregnant women from 4 to 10 mouse units of the hormone appear in the urine in 24 hours beginning about 5 days before menstruation and reaching the acme immediately before menstruation. In menstruating sterile women (husbands potent) free from inflammatory disease and with no obstruction of the tubes twenty-nine tests made during the 10 day period preceding menstruation showed only one positive, whereas in a group of forty-six normal women, thirty-two, or 69.5 per cent were positive, and in those functionally sterile only 3.4 per cent were positive.

In a large number of amenorrheic women two groups were distinguished by means of the blood and urine test. In the first, no cyclic accumulation of sex hormone can be demonstrated. In the second, an accumulation of hormone in the blood can be demonstrated in distinctly diminished amount.

"These observations warrant the deduction that the amount of female sex hormone produced is not necessarily an accurate index of the quantitative effects to be expected. The effect produced will depend on at least three factors: (1) the amount secreted; (2) the rapidity with which the hormone is utilized or fixed in the genital tract (as previously mentioned, it is as yet unknown whether during its utilization the hormone is fixed in the genital tract, utilized and then excreted or destroyed); (3) the rate and level (threshold) at which the excretion takes place.

"To recapitulate, we have noted that, particularly in the sterile and amenorrheic groups, the renal threshold (perhaps also the intestinal threshold, which has not yet been studied in these cases) is persistently and

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recognizably lowered. The hormone appears to be excreted with sufficient rapidity and in such amount as to cause a reduction of its concentration in the circulating blood. Consequently, in spite of functioning ovaries, little effect on the sex tract is produced. In the one group, amenorrhea with comparative lack of uterine function is noted; in the other, sterility due to insufficient pregravid (premenstrual) uterine reaction results."

The idea developed by Frank and Goldberger relative to renal permeability for hormones and the possibility of a lowering of the threshold sufficient to prevent the normal action of these hormones is a very practical one. In such a cyclic physiological phenomenon as menstruation which depends upon the attainment of a certain maximum concentration of hormone the effect of lowered renal permeability preventing such concentration is obvious. It seems possible, also, that the idea might easily be extended to other hormones which are slowly elaborated in small quantities during the 24 hour period. Constant removal by the kidneys of thyroid hormone from the blood might conceivably result in hypothyroid symptoms and consequent compensatory enlargement of the thyroid gland. Frank and Goldberger state that there is some evidence of such a reduction of the hormone level of the anterior pituitary, which appears in the urine and they say:

"On the basis of these observations, with all due reserve, we propound the query whether not only the female sex hormone and pituitary hormone but also other internal secretions may be excreted by the kidneys and other emunctories. If this hypothesis obtains, a balance between the amount secreted, utilized and excreted must be drawn in every instance to evaluate the physiologic effects to be looked for, as well as to govern the dosage in organotherapy."

The demonstrated existence of a changeable renal threshold for sex hormone opens up a promising field of research. The therapy of endocrine diseases and the use of endocrine products in medicine might undergo marked change if variations in hormones are due not to defects of elaboration but to variations in the capacity of the kidney to retain them.

1. Frank, R. T., and Goldberger, M. A., *J. Am. Med. Assn.*, 94, 1197, Apr. 19, 1930.

Abstracts

Severe Case of Diabetes Improved by the Administration of Salts of Nickel and Cobalt Simultaneously with Insulin.—Roch and A. duBois. (*Bull. et Mém. Soc. méd. Hôp. Paris*, **45** : 412, 1929.)

Up to the present only in cases of relatively slight degrees of diabetes were results obtained with the administration of nickel and cobalt, while in more severe cases this therapy remained unsuccessful.

The author observed a severe case of diabetes in which, during 24 days of insulin therapy coincidently 20 gr. of nickel chloride and cobalt chloride in solution, each 0.04 gr. in 10 parts of water, was given twice daily with very pronounced results. The condition of the patient 8 days after the commencement of this therapy was very much improved and lasted for many months. It would naturally be of practical value, if by means of small doses of nickel and cobalt, the use of insulin might be modified in the diabetic without any resulting harmful effect on the organism.

Communications on the Activity of the Hormone of the Anterior Lobe of the Pituitary.—Max Reiss and Käthe Langendorf. (*Endokrinologie*, **3** : 161, 1929.)

According to the authors' investigations the sex hormone of the anterior lobe of the pituitary acts on the genital system of female dogs and rabbits, producing changes similar to those already observed in rats and mice.

The corpora lutea maturing under the

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action of the anterior lobe hormone are genuine corpora lutea ("epitheliala"). The hormone of the anterior lobe of the pituitary affects cholesterin metabolism of normal female rabbits and dogs, so as to increase blood cholesterin. The increase comes about indirectly through the ovary. In ovariectomized animals the increase does not occur, it is lacking if there is no follicle in the ovary.

A definite effect of pituitrin on blood cholesterin could not be determined.

Concerning the Influence of the Anterior Lobe Hormone on the Respiratory Metabolism of Rabbits. — Max Reiss and Anton Winter. (*Endokrinologie*, **3** : 174, 1929.)

The authors injected doses of hormone between 200 and 4000 mouse units, in which the mouse units consisted of the smallest amounts that were able to bring forth follicular ripening and ejection into the ovary, hypertrophy of the uterus and stratum, within 100 hours, in the infantile mouse, by means of six injections divided between 2 days. From their investigations the authors could not establish any effect on the respiratory metabolism with any certainty.

Concerning the Manner of Acting of the Thyroid Gland Hormone. — Rudolf Weil. (*Klin. Wochenschr.*, **8** : 652, 1929.)

Tests with synthetic thyroxin (Scherling). Since it was determined that thyroxin itself does not possess a proteolytic property, nor affect the enzymatic splitting-up of albumin *in vitro*, through the direct effect on the ferment, proferment or substrate, the author investigated the course of tissue autolysis after dosage with thyroxin *in vitro*. Hence it was shown that thyroxin in very small amounts affects a quantitative increase of autolysis in guinea pig liver, in neutral reactions, in a dilution of 1:400,000 it causes an increase of over 50 per cent in 24 hours.

This finding only supports the interpretation that thyroxin starts a colloid-chemical change of cell structure, in the sense of an increase of degree of permeability of the marginal surface, which leads either to an improvement in the power of the ferment to attack (through liberation of adsorption agglutinins, increase of spacial dissociation of ferment and substrate), or to a disturbance of the reaction equilibrium (modification of the split products). Both factors depend, however, on the intensity of the enzymatic splitting-up of albumin.

Somatic and Autonomic Innervation. — Leo Hess. *Wien. klin. Wochenschr.*, **42** : 353, 1929.)

The presentation that in experiment, the hormones adrenalin and hypophysin effect a contrary, constricting or dilatating action, according to the condition of the cell walls of the blood vessels and exercise a reaction process on them, is interesting; correspondingly, the constricting action and the blood pressure effect occasionally fail in human beings.

The autonomic nervous system and its accessory organs prove to be — eventually with the aid of sensibilitizing substances — susceptible to the hormone. On the other hand the production of hormone is regulated by the autonomic nervous impulse. Adrenalin and hypophysin, for example, act not only on the definite nerves but also directly on the smooth musculature of the blood vessels, the ureter, etc. A modification of the somatic innervation by means of the hormone was not ascertained.

Asthma. Pharmacodynamic Treatment of Asthma Symptom Particularly by Means of Adrenalin and Ephedrin. — Zunz. (*Bruxelles méd.*, **9** : 924, 1929.)

Adrenalin is the medium which acts in truly dilating manner on the bronchi. By means of experimental research the activity of adrenalin is measured and it is shown that this is greater the stronger the contraction of the fibers. Ephedrin has an advantage over adrenalin: warm, it is more stable, it does not lose its activity with *per os* administration, and acts, though a little more rapidly, with a more lasting effect than adrenalin. Besides, increase in blood pressure was never observed with ephedrin. It has been shown experimentally that ephedrin acts directly on the nerve fibers, and cure by ephedrin has been cited by several authors.

Contributions to the Biology of Extractive Substances from the Cells and Tissues. — Ferd. Winkler and Franz Köck. (*Zentr. inn. Med.*, **50** : 610, 1929.)

In the course of an undertaking for the purpose of obtaining pure hormone the authors have contributed the following findings:

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1. The extractive substances gave no albumin reaction immediately after they were derived, but after several days there occurred a significant albumin reaction despite sterile preservation.

2. Freshly made preparations are white or light yellow, but darken under the influence of light. Also the original light preparations yield a dark color with Agaricus melleus-tyrosinase in weakly alkaline tyrosine solution.

3. Another extractive substance could be obtained from the female sex glands which differed from that obtained from the male and the extractive substance derived from the ovarian stroma was differentiated from that derived from the corpora lutea. The extractive substance derived from the sex organs exercises not only an entirely stimulating effect on the sex impulse but also induces a definite augmentation of the external genitals. The increase in libido is so great that a male mouse, quite weak, when treated with this hormone in captivity, promptly usurped the sex function.

4. From the heart of animals previously sacrificed after suitable preparation of the musculature according to the method of the authors, an extractive substance was derived which, similar to that of Haberlandt, was able either to quiet the heart or to cause it to beat. The substance obtained by the authors from the liver has not only an insulin effect but also a striking growth promoting effect; this liver substance also has a favorable effect on heart activity.

The extractive substance which was obtained from the tonsils has a stimulating effect on the blood-forming system. The extract from the lymph glands acts likewise. The extractive substance derived from the spleen has besides an influence on the hematopoietic system, another individual effect in the sense of an instigator of blood coagulation and also in the sense of an influence on heart activity. The extractive substance derived from the thymus has a similar effect. An active insulin was derived from the pancreas and with simultaneous extraction of pancreas and brain, an extractive substance which exhibited particularly intensified insulin effect was obtained.

Resistance to Incretion. — W. Falta. (*Wien. med. Wochenschr.*, **79** : 852, 1929.)

In healthy persons Högler and Holler have noted that large amounts of thyroxin do not affect either the basal metabolism or the cardiovascular apparatus. In obesity thyroxin medication is only to be reckoned if the calorie administration is diminished, as Falta shows by diagram. Plummer has contributed that thyroxin in Morbus Basedowi does not act if the basal metabolism has reached about 60 per cent. Observations of Falta and Bauer confirm this assumption. According to Falta's observations the effect is lacking in exogenous thyroxin. The sum total of all observations which have been initiated by pituitrin and insulin, advance the question as to whether the resistance to incretion is not conditioned by a stronger counter-regulation. It is not possible in every case to reduce the effect of the incretion to a simple form.

Concerning Resistance to Incretion. — Jehle. (*Wien. klin. Wochenschr.*, **42** : 823, 1929.)

The slight virulence of large doses of thyroid gland in children suggested the idea that this might chiefly be due to inactive substance. On this ground the excretion of water through the lungs under the influence of thyroid gland was tested. Tests were made on normal children as well as on nephritics and epileptics. The individual experiment on more than a hundred cases has not yet been concluded. It appears that under the influence of thyroid gland medication the water content of inspired air is definitely increased, yet after several weeks it again falls back to normal. From this it may be deduced that in spite of relative non-toxicity, thyroid gland medication is ineffective and perhaps this finding forms the explanation of the fact previously offered by the author, that there may be a process of dehydration in nephritics although neither increase of diuresis nor of sweating could be observed which would clarify the process of dehydration with loss of weight.

Concerning Resistance to Incretion. — W. Falta and F. Högler. (*Wien. klin. Wochenschr.*, **42** : 823, 1929.)

Numerous observations have already been made concerning resistance to incretions, for example, in diabetes insipidus against pituitrin or in diabetes mellitus against insulin. There are also older contributions concerning the resistance to thyroid gland substance, particularly in children and young animals. The authors report on two cases of a high

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degree of resistance to thyroxin in adult individuals (one case of evident lues affecting the brain — a Parkinsonian). This individual was not resistant to thyroxin derived endogenously, since no myxedematous symptoms were evident and the basal metabolism was normal. Entirely analogous observations may be made in the case of resistance of diabetics to insulin. A demonstration of such a case was given. The question of resistance to incretion was seen by the authors to be a counter-regulation chiefly released through the central nervous agency. In the case of diabetes the problem must above all be concerned with a release of suprarenal activity. An analogous circumstance of resistance to thyroxin could be demonstrated in animal experiments.

Concerning Hyperthyrosis and Its Treatment with Micro-Iodin Doses. — Martin Engländer. (*Würzburger Abhandl. Gesamtgeb. Med.*, **6** : 1, 1929.)

The author takes sides with the theory that iodin is the chemical or physical principle present in the thyroid gland hormone. The decreased function can be greatly influenced by means of micro-doses of iodin alone, there is no practical advantage in the repetition of the curves. Apathic persons lacking energy recover under this cure, become anxious to work and are capable. The thyroid gland hormone is the strongest dynamic principle in the sense of a catalyzer. The therapy with micro-doses of iodin differs from thyroid gland therapy in that it does not have the effect of rapid oxidation of fat. The author never observed emaciation with micro-doses of iodin.

Thyroid Gland Tablets in Persons with Hypertonia. — B. Molnar. (*Therap. Gegenw.*, **70** : 191, 1929.)

The author presents the observation on a certain form of high blood pressure, in which thyroid gland tablets were administered with success. Evidently the thyroid gland tablets further oxidation increase and besides act to reduce obesity. In patients with essential hypertonia who suffer from joint edema, there are two symptoms, namely obesity and edema, which give indication for thyroid medication; the third symptom, hypertonia, does not. Nevertheless, the author treated thirteen patients of this sort, with blood pressure up to 210 mm., very cautiously, to be sure, with thyroid gland medication 0.10 gr. each beginning with ½ tablet and advancing to twice a day 1½ tablets). In every case there was decrease in body weight, significant lowering of the blood pressure and disappearance of the edema. By means of thyroid gland treatment the blood pressure decreases were accounted as intoxication symptoms and in such cases the medication is recommended. The author never observed any secondary effect which would make cessation of the treatment desirable. It is, of course, compulsory that dosage be given cautiously.

The Physiology and Pathology of Blood Coagulation. c. Hormone-Coagulation and Gland Function. — Edgar Wöhlisch. (*Ergebn. Physiol.*, **28** : 588, 1929.)

According to the investigations of Cannon and Gray, adrenalin in small doses administered intravenously (0.001 mg. per kg.) and in somewhat larger doses administered subcutaneously, shortens the coagulation time to ⅓ the normal value. By means of the extracts of the anterior and posterior lobes of the pituitary the blood coagulation should be influenced in the opposite way. According to J. la Barre the coagulation-promoting extract of the posterior lobe considerably accelerates the formation of thrombin, also the effect of thrombin on fibrinogen was rather favorable. The anterior lobe extract defers all phases of coagulation as does also cholin.

According to Ischikawa and Sasaki the coagulation time in rabbits gradually increases with the feeding of thyroid gland, likewise the fibrinogen content of the plasma. Cantarow, Cauen and Gordon report on an investigation with subcutaneous administration of Collip's parathyroid hormone in healthy persons. They found — by no means constantly demonstrable — a transitory increase of serum calcium, a slow rising of the blood calcium and an acceleration of the blood coagulation. Wohlgemuth and Hiruma found that after ligature of the pancreas duct the fibrinogen content of the blood rises 2 to 8 times the normal value, while the thrombin content of the serum remains unchanged. Parallel with the increase of fibrinogen there occurs a retardation of the coagulation process. La Barre shows that impure insulin preparations, with regard to their cholin content, inhibit the change of proserozyme to serozyme as well as the reaction of the serozyme with the

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...ertozyme. Pure insulin should not disclose this effect.

Concerning the Appearance of Sugar in the Urine with Insulin Injections. — Ernst Wichmann. (*Deut. Arch. klin. Med.*, 164 : 172, 1929.)

In a patient with icterus in whom there was demonstrable, at the height of the icterus, a diabetes among other disturbances of the carbohydrate metabolism of the liver, up to 17.6 gm. sugar per day were excreted in the urine after injections of insulin. The blood sugar was maintained at the lowest normal limit. After abatement of the icterus despite continuous insulin dosage, no more sugar was excreted into the urine. The author maintains that it is possible that in icteric patients, the insulin induces an electrolyte displacement in the blood or an altered formation of sugar in the blood. At any rate, with the administration of insulin in the treatment of non-diabetic patients, the appearance of sugar in the urine is henceforth to be expected.

Concerning the Antagonistic Relationship between Posterior Pituitary Hormone and Insulin. — Karl Velhagen. (*Arch. exp. Path. u. Pharmakol.*, **142** : 127, 1929.)

The investigation conducted by the author offers adverse testimony for the fact that insulin is an antagonist of the uterus-exciting and blood pressure-increasing hormone of the posterior lobe of the pituitary.

The blood sugar-increasing and insulin-antagonistic substance of the posterior lobe is contained in the pars neuralis as well as the pars intermedia. In order to inhibit the insulin hypoglycemia very large quantities of substance from the posterior lobe must be administered. Likewise, by means of repeated dosage of extract of the posterior lobe the action of insulin originating in the body is not suppressed. No diabetes mellitus occurs. Pituitary glycosuria can not be derived from increased dosage of posterior lobe secretion and therewith the particular inhibition of insulin action can not be increased. The secondary hypoglycemia which is often to be observed after administration of posterior lobe substance is probably the result of an enlarged insulin secretion. In animals with pancreatic diabetes the secondary hypoglycemia is lacking.

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Concerning the Action of Kidney Extracts on the Functional Status of Contracted Kidney. — Stejskal. (*Med. Klin.*, **25** : 983, 1929.)

A systematic organotherapy in diseases of the kidney by means of internal administration of kidney extracts was first instituted by Dieulafoy (1892).

The author obtained results with parenteral administration of kidney extracts in ten cases of primary and secondary kidney contraction which are of interest and have a general significance. The kidney extract was administered partly in the form of watery extracts and partly in such a form that the lipoid substance of the kidney was contained in non-autolysated form. This was administered to the patient in the form of an intracutaneous blister in amount from 2 to 5 cc., in order to insure slow resorption of the extract. The fact was brought out that, excluding any disturbing general reaction of the organism, the method of treatment was capable of suppressing the increased blood pressure of hypertonia which occurs in kidney diseases (primary and secondary kidney contraction). The influences on the blood pressure are organ-specific, *i. e.*, they occur only after injection of kidney extract and only in nephritic hypertonia. Decrease of polyuria was observed four times. The decrease of blood pressure in contracted kidney will also serve as a valuable therapeutic indication. Whether there is a relationship between the substance in kidney extract and the circulation hormone found in the urine by Frey, can not yet be stated. The most important fact of this contribution is the information that lipoid extracts of kidney also act on the blood pressure in contraction of the kidney.

New Therapeutic Investigations on Hydrops Articulorum Intermittens. — Hermann Schlesinger. (*Wien. klin. Wochenschr.*, **42** : 832, 1929.)

Up to the present time only a few more than a hundred cases of this disease have been known, of which number the author was able to observe fifteen (in 25 years). Only two of the patients were males. The cyclic course of the joint swellings was quite regularly interrupted by pregnancy. The author assumes a hormone dependence which is evident as a functional anomaly of the ovary. During pregnancy part of the function of the ovary is consigned to the placenta and the effect of the hormone produced by this agent is a much stronger one than that of the ovary. Following upon the improved function or the increased function, the swellings cease. The accuracy of this hypothetical explanation is supported by the therapeutic effect which was obtained by means of subcutaneous injection of placenta extract.

How Does One Treat Nervous Congestion and Sweating? — Spiegel. (*Mitt. Volksgesundheits.*, No. 6, 194, 1929.)

Besides a general quieting effect, an influence by means of ovarian and testicular preparations may be expected for disturbances of internal secretion (hyperthyroidism, hypofunction of the genitals) and a suitable therapy is to be obtained.

Concerning the Influence of Thyroid Gland Activity on the Depression of Red Blood Corpuscles. — E. P. Tschernosatonskaya. (*Zeitschr. ges. exp. Med.*, 66 : 67, 1929.)

The speed of depression of blood corpuscles was studied in normal and thyreoprivic animals.

After thyroidectomy the reaction slows down so that the maximum retardation occurs 4 to 6 weeks after the operation.

After feeding of thyroid gland, depending upon the dosage, there occurs an acceleration of depression speed, of pulse, and an augmentation of lymphocytosis.

Lugol's solution in small doses has the same effect, but in slighter degree. The changes in depression speed can perhaps serve as an evaluation method for thyroid preparations.

The Influence of the Male Sex Hormone on the Female Organs of Generation and on Gestation Processes. Hormonal Sterilization and Interruption of Pregnancy in Female Animals. — Wolde-mar Reiprich. (*Arch. Gynäkol.*, 136: 417, 1929.)

The incretory influence of male sex hormone on the generation processes and generative glands was studied by means of twenty-five transplantations of testicle on female rabbits. It was possible to obtain by transplantation of fresh testicle tissue, hormone sterilization as well as interruption of pregnancy in female animals. The smallest effec-

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tive amount (in rabbits) was about one-half a mature testicle, a positive effect was only to be obtained in the first half of pregnancy. In the case of successful pregnancy, a striking decrease in the number of offspring occurred with insufficient hormonal activity of the male sex hormone administered with the sex glands. The pathological-anatomical findings were: striking atrophy of the internal female genitals. In the gravid woman hormonal interception is not possible up to the present time. The investigation forms further positive proof for the laws of antagonism of the gonads.

On the Question of Endocrine Arthritis (Eunuchoidism and Morbus Bechterewi). — Jakob Ratner. (*Mitt. Grenzgeb. Med. u. Chir.*, **41** : 402, 1929.)

In a patient with typical eunuchoidism there existed spondylarthritis ankylopoietica. The question of whether it was an endocrine arthritis depends upon whether one can speak of an endocrine disease, if endocrine therapy serves good stead. In this sense one can speak of an endocrine arthritis. Although J. Bauer cautions against too great optimism with regard to endocrine therapy, he unjustly restricts the limits of this therapy. In order to know what this therapy is actually able to accomplish we must take every advantage of it and deliberate upon it profoundly.

Organ Extracts and Their Effect on Immuno-Biological Processes. — Pockels. (*Med. Klin.*, **25** : 975, 1929.)

Spleen and lung extracts were given *per os* to human beings to maintain the active di-immunization. A specific influence was derived.

Concerning the Effect of Parathyroid Extract on the Formation of Blood. — Stephan Pelláthy and Josef von Fernbach. (*Endokrinologie*, **3** : 406, 1929.)

The authors have investigated the effect of the Collip extract Parathormone on the formation of blood in various patients. The investigations show that the Parathormone exercises a positive effect on the formation of blood and that the effect evidently may be considered as hormonal, not as calcium activity, since it still remains when the calcium content of the blood is not raised, or in other words, since the changes observed are different from those described by other authors after administration of calcium. The red blood cell count suffered no significant change. The test was performed to count the white blood cells in five asthmatics, seven Basedow patients and in fourteen other patients after injection of Parathormone.

It was shown that with the administration of Parathormone an increase in count of myeloid cells occurs similar to that after adrenalin and thyroidin. There are similar changes in formation of the blood after stimulation of the sympathicus, when a leucocytosis exists. In as much as the sympathetic and parasympathetic formation of blood may be contrasted with each other, the action of parathyroid extract may be indicated as sympathicotonic; hence it can also be of value in that favorable results are to be obtained when it is administered in vagotonic diseases, in asthma, urticaria and serum sickness.

How May the Favorable Effect of Liver Therapy Be Explained? — J. Pal. (*Mitt. Volksgesundheits.*, No. 6, 194, 1929.)

Liver contains substances from the realm of the amines, which promote the formation of erythrocytes in the bone marrow, provided the bone marrow may be influenced. All kinds of liver which have been investigated up to the present have proved to be effective in suitable amounts, for example, even fish liver. On the quantitative basis calf liver, pig liver and ox liver are just as appropriate as bird liver. Fatty liver is not to be recommended since the same weight contains much less active substance. The administration of extracts simplifies the treatment.

Concerning the Effect of Spleen Extract on the Formation of Red Blood, Particularly in Hyperglobulia Vera. — Nipperdey. (*Deut. med. Wochenschr.*, **55**: 1085, 1929.)

The experiments of the author show that the extract form of spleen therapy, as far as concerns dosage and compatibility over a long period, is apparently simple, that to a great extent the subjective improvement was very much pronounced in all patients, in whom there occurred a considerable increase in weight. The dosage varied individually. With too small doses extensive objective harm may be caused by a polycythemia. This

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result shows that, according to the severity of the disease, the length of time it has existed and the age of the patient, the results of spleen therapy must be various. According to the reports given, up to the present, the therapy is exhausted, not in the transitory result of short periodic administration, but with proper dosage, without calling forth any harmful effects, it appears to have a better effect if administered longer.

The Effect of Liver Extract on the Disturbance of Diuresis in Kidney Insufficiency. — Hans Molitor and S. Glaubach. (*Wien. klin. Wochenschr.*, **42** : 889, 1929.)

From the cortex of the liver, by means of fractionated extraction according to a certain process, various liver preparations could be obtained which partly caused a diuresis-inhibiting, partly diuresis-promoting effect. It was shown in dogs with decrease of kidney parenchyma to one-quarter efficiency, that the water metabolism, after subcutaneous injection of 10 to 20 mg. of the liver extract, was almost without exception altered so that there was an increase in amount of excreted urine toward normal values and therewith an improvement in the general condition. The liver preparation acts in amounts of from 1 to 2 mg. per kg. of animal, it is water-soluble, has only a weak albumin content, is free from lipoids, bile acids and purin derivatives.

The Administration of Insulin in Oily Suspension. — O. Leyton. (*Bull. et mém. Soc. méd. hôp. Paris*, **45** : 779, 1929.)

The subject of the author is the administration of insulin in oily suspension. After numerous investigations with other oils, castor oil was found to be the most suitable. This oil can carry 100 units of suspended insulin per cc. Owing to its low degree of viscosity the oil must be heated slightly before the injection. The needle used for the injection can not be so fine as that used for watery solutions. The most important fact is that the injection be given not intramuscularly, but subcutaneously. It has been observed that these are the least painful. It is given in the morning before the patient rises. The author is satisfied with the results obtained with this method and he believes that other hormones may be applied with advantage in the same manner.

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Pharmacology with Reference to the Intestine. — Hans Molitor. (*Wien. klin. Wochenschr.*, **42** : 839, 1929.)

Adrenalin, the stimulating medium of the sympathetic, has hardly any value in administration to quiet the intestine; however, it is noteworthy that it could be observed in human beings, that each state of excitation, which evidently leads to an increased endogenous adrenalin production, is followed by a protraction of intestinal movement. The secretion of intestinal juice is regulated (at least in part) by a hormone, that is by means of secretin which is chiefly formed in the pars pylorica, and is released from this place into the blood stream to the intestinal glands in the fundus.

Leading Theories on the Treatment of So-Called Pyloric Spasm. — H. Mettenheim. (*Med. Welt*, **3** : 887, 1929.)

The existing disturbance of equilibrium of the vegetative nervous system can be based upon a weakness of the sympathetic; thus Paul (Frankfurter Children's Clinic) recommends injecting intracutaneously 4 to 5 times daily, shortly before meals, from 1 to 2 parts of a 1:1000 adrenalin solution. The effect lasts about 40 minutes. This therapy has been confirmed by the author as well as by other reporters (Finkelstein).

In the Treatment of Hyperemesis Gravidarum Can Insulin Be Substituted by Synthalin? — Köhler. (*Mitt. Volksgesundheits.*, No. 7, 227, 1929.)

A substitute for insulin in the treatment of hyperemesis does not seem to be entirely recommendable. Synthalin is not to be regarded as an absolutely harmless medium for there have already been several cases of injury to the liver after use of this substance. Since hyperemesis as well as other toxicoses of pregnancy are quite commonly associated with injury to the liver, synthalin medication would act as an additional injurious agent, which must be avoided.

The Treatment of Diseases of the Liver with Insulin and Grape Sugar with Regard to Young Children. — Knake. (*Zeitschr. Kinderheilk.*, **47** : No. 5, 1929.)

Simultaneous administration of insulin and grape sugar was used in severe symptoms of liver insufficiency and in slight cases of parenchymatous disease of the liver, for the purpose of maintaining or increasing the function of the liver for the final glycogen stage. Favorable results were obtained in the case of an 8 year old syphilitic girl, very icteric, with signs of severe liver damage which were to be accounted as acute yellow atrophy of the liver.

The Natural Immunity of the Child and the Possibility of Influencing It. — H. Kleinschmidt. (*Jahreskurse ärztl. Fortb.*, **20** : 17, 1929.)

Under the investigations for artificially increasing the natural immunity experiments with organ extracts are also to be mentioned. Recently interest has been directed to spleen extracts. The experimental foundations are at any rate very far-reaching. By means of prophylactically and therapeutically administered injections, Schröder was able to obtain a rise in resistance in tuberculosis-infected guinea pigs. In primary vaccination of guinea pigs Schlack found a definitely stronger, more lasting, and in secondary vaccination, a definitely weaker, more abrupt reaction than was exhibited by the controls. Thus an increased prophylaxis and hence also a stronger immunity was obtained by means of spleen extract.

Clinical and Experimental Observations on the Ovarian Hormone Folliculin. — S. Joseph and I. Raschkes. (*Deut. med. Wochenschr.*, **55** : 1044, 1929.)

Amenorrhea due to subfunctioning of the ovaries was improved in a portion of the cases by folliculin injections over a long period. Folliculin has the best effect in young operatively castrated individuals, in whom the therapy is commenced as soon as possible after castration. The choice of female patients is important for the success of the therapy, particularly in cases where associated diseases of other glands are to be expected. Intramuscular injection is as effective as intravenous.

The Action of Extracts of Endocrine Glands and of the Cardiovascular System of Warm-Blooded Animals on the Heart of Warm-Blooded Animals, *in Situ*. — G. J. Katz and E. A. Liebenson. (*Paris méd.*, **19** : 590, 1929.)

The authors worked with extracts of the following (14) organs: Right and left ven-

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tricles, heart auricles, vena pulmonis, aorta, lungs, bronchioles, liver, kidney, suprarenals, thyroid, testes, pancreas and spleen. The authors studied the effect on the heart *in situ* of a mixture of all of these extracts given by intravenous injection. For comparison, extracts of the ox, horse, dog and gull were derived. An experimental series was established with each one of these mixtures. The authors experimented with cats, dogs, rabbits and guinea pigs. In the investigations on cat hearts the authors found that the administration of the combined extract intensified the positive inotropic, and in the majority of the cases, also the positive chronotropic action of the heart. If the animals were previously chloroformed the combined extract strengthened the neuro-muscular system of the heart and made it more resistant. After preliminary nicotin injection the chronotropic action of the heart was first negative and then positive. Chlorammonium preceding the injection of the extract led to acceleration of the contraction and to its intensification. After previous treatment with morphine the contraction was likewise particularly strong.

A Clinical Method for the Assay of Insulin Preparations. — Karl Csepai and Bela Förstner. (*Endokrinologie*, **3** : 412, 1929.)

The method is based on the idea that the persistence of sensibility to insulin in one and the same person can be assayed so that it may be possible to control various insulin preparations as well as to estimate the sensitivity of a person to various insulin preparations. The effect of a freshly prepared solution of international insulin in the proportion of 1/15 unit per 1 kg. of body weight was tested on a chosen individual and on the third day thereafter the same amount of the insulin to be tested was given. By means of comparative curves it was possible to obtain relatively exact information as to the content of specific substance of the preparation in question.

An Essential Aspect of the Problem of Medical Application of Insulin. The Question of Degree of Purification of the Insulin Preparation. — H. Chabanier, C. Lobo-Onell, M. Lebert and E. Lelu. (*Presse méd.*, **37** : 766, 1929.)

For the purpose of successful antidiabetic treatment the entire diabetic process must be influenced, *i. e.* the acetonuria, the glycosuria and the hyperglycemia. And then care must be exercised that these symptoms do not return again. This is quite possible with only slightly purified insulin, which permits the interception of the symptoms and, in itself, is not dangerous. The result is otherwise with intensely purified preparations. Only small doses, such as are required in slight cases, and here, too, it was not difficult to correct the symptoms, were well tolerated by the patients. In cases of medium severity and in intense cases, in which one is forced to increase the dosage, secondary effects often occur which are prompted by the increased dosage. The difficulty of treatment lies in the fact that on the one hand the dosage chosen must be large enough to be effective and secondly, secondary symptoms must be avoided. The fact arises that with systematic treatment of diabetes with insulin only certain symptoms retire while others, for example the glycosuria and the acetonuria, still remain. In this instance very little has been accomplished with insulin. The success of the therapy rests with the adequacy of the dosage.

Concerning a Case of Acne Rosacea Accompanied by Endocrine Disturbances. — Bory. (*Progrès méd.*, **57** : 1011, 1929.)

In a 42 year old female patient who had suffered from obstipation for a long time, had been dyspeptic for 6 months and for 13 years was afflicted with a pustular cutaneous eruption of the face and a facial erythrosis, there were present all indications of a Raynaud symptom complex (numbness in the finger, violet color of the nose). The patient only began to menstruate at the seventeenth year, and at 40 reached the menopause, hence there was evidence of ovarian disturbances. Besides local medication and attempts to alleviate the dyspeptic symptoms, the patient also received pluriglandular therapy, namely thyroid gland, ovarian and testicular substance. More will be reported later concerning the ensuing process.

Concerning Cases of Pernicious Anemia Which Appeared Refractory to Liver. — Léon Blum and C. van Caulaert. (*Progrès méd.*, **57** : 1055, 1929.)

Report on cases of pernicious anemia which were left absolutely uninfluenced after certain liver extracts, while they reacted favorably to calves' liver and also to other extracts. The

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necessity of strict control of the activity of liver extract is stressed.

Unusual Insulin Damages to the Circulation and the Effect of Them on Carbohydrate Metabolism. — Reinwein. (*Dtsch. med. Wochenschr.*, **55** : 951, 1929.)

From two case histories it was shown that in insulin treatment of diabetics with heart trouble the effect of insulin on water maintenance must not go unconsidered, if one does not wish to expose the patient to the danger of increasing or causing an insufficiency of circulation. If such does occur, then the activity of the insulin is greatly lessened and the carbohydrate tolerance will be made much worse by large insulin doses.

Remarks on the Influence of Liver Substances on the Formed Elements of the Blood. — N. Reinitz. (*Skandinav. Arch. Physiol.*, **56** : 1, 1929.)

By means of investigations on healthy rabbits the author tested the influence of liver substances on the formed elements of the blood. It is thus shown that by intravenous injections of liver extracts an intense thrombocytosis as well as a weak lymphocytosis may be induced. In two instances the polymorphonuclears also showed a slight increase. As opposed to this, the injections produced no changes in the erythrocytes of healthy animals. Watery as well as alcoholic liver extracts are active, the former perhaps more so than the latter. Under certain circumstances liver extract can exercise a strong toxic effect, since it very rapidly induces respiratory paralysis during continuous heart activity. In normal animals liver extract is without effect on the erythrocytes and on the hemoglobin content. The occurrence of thrombocytosis implies that the liver extract exerts a stimulating effect on the red marrow.

Effects of Acetylcholin on the Secretion of the Pancreas. — Maurice Villaret, L. Justin-Besançon and Roger Even. (*Paris méd.*, **19** : 501, 1929.)

Inspired by the investigations of Desgret and the later investigations of Launoy, the authors studied the action of subcutaneous and intravenous injections of acetylcholin on the pancreas secretion in dogs. They observed that this substance causes the secretion of a juice which acts upon egg albumin and hence contains a primarily active trypsin. By means of ligature of the duct of Wirsung (pancreatic duct) and following this by injection of acetylcholin, similar to the experiments made by Binet and Brocq with pilocarpin, the authors essayed to induce a hemorrhagic pancreatitis. Once out of four attempts they obtained a pancreatitis with hemorrhagia and fat necrosis.

Functional Test of Blood Circulation. — Usadel. (*Therap. Gegenw.*, **70** : 224, 1929.)

The author gave hypophysin intravenously before operations in order to determine its action on the circulation. In healthy individuals a typical curve was obtained and in these cases the operation proceeded without any disturbance; in cases with an atypical curve, disturbances in the form of cardiac weakness occurred after the operation.

Influence of Thyroid Gland and Pancreas on the Carbohydrate Metabolism of the Liver. — Rudolf Siegel. (*Klin. Wochenschr.*, **8** : 1069, 1929.)

The disturbance of metabolism in diabetes is wholly and entirely to be considered as a deficiency of insulin in the organism. Nevertheless, we see how by means of impaired function the disorders of the endocrine glands come about, which have different characteristics for each organ investigated. The distortion of correlation occurring mostly in diabetes affects the ratio, to be counterbalanced, with regard to utilization of carbohydrate in metabolism in the thyroid gland and insulin effects in the end-organ. Since in the liver this antagonism is particularly important vitally, the disturbance of metabolism of the liver in the diabetic organism appears in the above defined form.

The Hammar Experiments concerning the Human Thymus. — B. de Rudder. (*Med. Klin.*, **25** : 812, 1929.)

Hammar's material comprises forty-six hyperplastic, post-fetal thymuses. In thirty-four instances there is evidently disturbance of the internal secretions. The predominance of disturbances of internal secretions with hyperplastic thymus presses the conclusion that the hyperplasia is only a symptom of an endocrine disease. The variable in thymus parenchyma is the leucocyte content and the presence of Hassall bodies. Leucocyte depression results in hypofunction or symptoms in the sex glands or suprarenals. Leucocyte

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excitation results in hyperfunction of the thyroid, and apparently also of parathyroid and pituitary.

Dietetic Stimulation Therapy. Concerning the Modern Treatment with Endocrine Glands. — Wilhelm Schlesinger. (*Wien. med. Wochenschr.*, **79** : 772, 1929.)

The investigations on the administration of vitamin and hormone present the conclusion that both of these substances function as a simple equivalent for the substance lacking in the organism, to activate protoplasm. Hormones as well as vitamins are thermolabile and hence all glands are effective if they are taken raw or only slightly cooked. In cases of latent malaria, in which proliferation of the gametes with true malarial symptoms were evident, the author instituted experiments with thymus and effected a stimulation with *per os* administration. Müller and Del Campo found increase of muscle activity after injections of thymus extract, Bier recommends thymus feeding in healing torpid processes; the action of thymus on bone growth is generally well known (Hass and Glässner). Gudernatsch and Romeis observed increase in propagation when tadpoles were fed thymus substance. This can lead to the investigation of the administration of thymus in hypofunction of the female sex glands. Birkler administered spleen in large amounts in various dermatoses and found a predominantly favorable influence in cases of neurodermatitis, and likewise in allergic conditions of the skin with definite eosinophilia. The results of administration of spleen in cases of tuberculosis are to be considered in the light of a stimulation therapy. The results of spleen therapy in tuberculosis of the bones accords with the finding of Meyer that after involution of the thymus the spleen takes up the function of the thymus. Liver which plays such an important part in the treatment of pernicious anemia, is extremely rich in ferments. Such ferments consist of, besides other factors, the power of forming amino acids, and thus the liver may be considered to be in direct co-operation in the formation of albumin and therewith the prevention of the formation of toxins in the blood, because of its ferment content. It is noteworthy that all authors are agreed that liver, as such, acts better than liver extract, and above all, the administration of heat must be moderate. Hence the active substances are thermolabile and this is consistent with the assumption that the liver ferment is the active agent.

The Action of Several Medicinal Preparations on the Function of the Stomach with Considerations of Blood Pressure, Pulse and Blood Formation. — Ernst Schwab. (*Zeitschr. ges. exp. Med.*, **65** : 782, 1929.)

The author conducted experiments on twenty-two patients to determine the effect on the function of the stomach of 0.01 mg. Suprarenin hydrochlor. synthet. Höchst.

In fifteen patients with no organic gastric disorder there was found six times reduction and five times increase of the acid values; in three cases there was no variation found in the trend of the curve. In five cases of Ulcus duodeni there always occurred decrease in the acid values. In one case of perriduodenal adhesions and in a case of Ulcus ventriculi there was a significant increase of acidity. In nine instances without organic gastric disorder the time of evacuation was increased by the administration of adrenalin, in three instances it was unchanged; in three cases of Ulcus duodeni it was deferred and twice it was increased. Influence of the amounts of secretion, of post secretion and of the duodenal reflux were not definitely determined. There was an increase in systolic blood pressure. The pulse was increased in three cases. The blood picture showed a definite increase in leucocytes. In general, nothing can be said for conclusive results as a functional test.

Relationship between Diseases of the Blood and Diseases of the Digestive Apparatus. — Emil Schwarz. (*Wien. med. Wochenschr.*, **79** : 738, 1929.)

The results of liver therapy in pernicious anemia are an indication that the toxic action as well as the so-called hemolytic process in pernicious anemia can be successful otherwise than has been assumed. The author does not agree with the broadened opinion of the day, that liver therapy is a simple symptomatic method, a stimulant for the bone marrow, and he assumes further that the liver has a specific rôle in the formation of the blood. Hence it is shown that the megaloblastic formation of blood in the embryo is released at the instant the normoblastic is released if the liver cells are differentiated from the primordial cells of the embryo and further that no

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other remission of pernicious anemia like that of liver feeding, permits the return to normoblastic, orthochromatic type.

Concerning the Action of Kidney Extracts on a Functional Basis in Contracted Kidney. — K. Steyskal. (*Wien. klin. Wochenschr.*, **42** : 696, 1929.)

In seven cases of part primary, part secondary kidney contraction, it could be shown that by means of intracutaneous injection the hypertonia of the kidney could be abated. In cases of non-nephritic hypertonia, kidney extract failed to act. Hence, it is a matter of specific organ effect of tissue extracts, which could likewise be called forth with lipoid extracts of the kidney.

The Whipple Cure and the Modern Treatment of Pernicious Anemia. — Paul Veran. (*Rev. méd.*, **46** : 325, 1929.)

Patients with pernicious anemia are not treated the same way in France as they are in America; other methods are used more often, such as blood transfusion and insulin therapy. The result is that the statistical data concerning liver therapy do not present the clear picture they do in America, where this treatment is given exclusively.

It is impossible to indicate either generally or specially the necessary duration of liver therapy. Recurrence of the disease or relapse due to intercurrent disease occurs occasionally, but these cases are always actively combated with the newer liver therapy. E. Bernard and Deslenquois, in a case of pernicious anemia due to bronchitis, have observed a diminution of red blood cells from 3.6 millions to 2.2 millions and a very abrupt rise of the erythrocytes occurred after liver therapy. Daily ingestion of liver has to be reinstituted each time the symptom reappears in the patient treated, hence liver extract will be of good service for the intermittent medication. After too lengthy use of excessive dosage, aggravation of the disease symptoms was observed. In a patient with kidney disease, who was undergoing liver treatment without the control of a physician, anemia occurred. Pal observed the occurrence of high arterial blood pressure in a patient who became erythremic. Hence consideration must be given to the problem of large doses of liver throughout a long period of time, lest adverse results ensue.

The practical significance of liver extract is great, nevertheless there is no adequate proof as yet, whether there is a definite advantage in the effect of liver extract.

Concerning the Advancement of Bone Growth by Means of Injections of Bone Extract. — Carla Zawisch-Ossensitz. (*Wien. klin. Wochenschr.*, **42** : 733, 1929.)

Comprehensive researches of the author give the following results:

In the bones of young animals, in particular those of animals in the period of greatest growth, there is present a ferment, which is in apposition with organic bone substance or promotes it and which is differentiated from the calcium phosphate designated (Robinson) hexosemonophosphate. The author was concerned with obtaining it in pure state.

By means of the injection of a bone extract containing the ferment, an improvement may be derived in the growth of bones of young animals. The action is not one of a stimulant, but is specific and could be initiated in animals of the same species as well as those of another.

Moreover, its administration causes no unpleasant secondary effects and since the extract is much more applicable locally than generally, there is nothing to hinder osteotherapeutic tests on human beings.

Estrous Hormone in the Bile. — M. A. Gsell-Busse. (*Arch. exp. Path. u. Pharmakol.*, **139** : 328, 1929.)

The author demonstrated that Na-taurocholate contains an active principle which acts in the manner of an ovarian hormone. Further investigations show that the action is not inherent in the acid taurocholate or in the acid bile salts. The estrus-producing action does not originate with the cholate either, but from a combination of cholates. The active substance is insoluble in pure water, but soluble in most lipoid mediums. Of the animal biles, ox bile is the best speculation. Hog and dog bile exhibit the lowest value of activity. Allen and Biedl found that there is no estrous hormone to be obtained from the placenta of hogs and dogs. In seventeen experiments with human bile, coming from women, all were active. Fourteen experiments on bile from men proved apparently less active than that from women. Further experiments were conducted with liver extracts from animals. It was found that the total lipoid extract of 0.5 kg. of fresh

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liver was not entirely inactive, that is, that 0.5 kg. of fresh liver did not contain 1 rat unit. In two instances of pregnancy no estrus-inducing substance was demonstrated. Meconium contains the greatest promise up to the present (1 kg. calculated to contain 6000 rat units). The author holds the opinion that the placenta as the place of origin of the estrus-inducing substance is not definitely determined and he considers the possibility that the embryo bile, that is the embryo liver, during pregnancy is the site of production of the estrus-inducing hormone.

Concerning a Hormone of Heart Motion. II. Contribution. Further Experimental Investigations with the Heart Hormone Preparation. — L. Haberlandt. (*Pflügers Arch. ges. Physiol.*, **221** : 576, 1929.)

In new tests with the heart hormone preparation which has recently been obtained histamin-free the pulse-inciting, pulse-accelerating and pulse-strengthening activities of the heart substance were demonstrated on isolated frog ventricles, using dilutions of 1:10 million; also the rhythmic and positive dromotropic effect observed in earlier experiments, in general were observed in frog hearts which had been isolated two days previous.

By means of suitable doses of the preparation the sensitivity of the frog heart chamber was increased so that with further dilution definite action of the heart was obtained. Such a sensitization could also be obtained with treatment of the animal for several days in the form of injections into the lumbar lymph sac.

Strong concentrations of heart hormone preparation, for example 1:100, can, under certain circumstances, but must not cause an inhibiting action.

The heart hormone preparation decreases the tendency of the frog ventricle to deteriorate with faradic stimulation of the atrioventricular region in surviving network.

Pharmacological Researches on the Heart Hormone Preparation. — L. Haberlandt. (*Med. Klin.*, **25** : 329, 1929.)

The investigations of the author have shown that the action of digitalis substance on frog hearts previously treated with heart hormone preparation, in the most cases, was increased, in contrast to the control hearts. In this instance the sensitizing effect of the heart hormone preparation was shown to be strongest with strophanthin, weaker with digipuratum, and weakest with squill. The clinical importance of sensitivity to digitalis substance obtained by means of heart hormone treatment is close at hand. Further it was demonstrated in another series of experiments that the capacity for resistance of the isolated frog heart against chloroform and ether narcoses after previous treatment with heart hormone preparation is, in general, greater, and its capacity to relax is increased. This rise in resistance to organ narcosis which has been demonstrated by means of the heart hormone preparation, will also be valuable in general narcosis, hence its practical value.

The Laurence-Biedl Symptom Complex. — Hertzog. (*Zeitschr. Augenheilk.*, 67 : 176, 1929.)

In two brothers suffering from obesity, dystrophia adiposogenitalis, polydactylism, disturbance of mental development and retinitis pigmentosa thyroid therapy was instituted with the result that in one patient the acuteness of vision was somewhat, and in the other very much improved.

Communications on the Initiation of Birth According to Stein. — Max Widers. (*Zentr. Gynäkol.*, **53** : 403, 1929.)

The process according to Stein, for initiating the birth process at the termination of pregnancy is as follows: In the morning early, two teaspoons of castor oil, 2 hours later 2 drops of pituitrin, and then twice every hour two drops of pituitrin were given. If at this point the labor pains began the pituitrin doses were resumed intramuscularly several times, with the result that the birth process was ended by evening. In failure to succeed the medication was instituted again on the second and third days and 60 to 70 per cent of the women reacted, *i. e.* if the uterus was actually capable of producing labor pains. The period of pregnancy must have reached its termination. This is a prerequisite. The reports on the matter are variable. Hatzky (Hamburg) reports 30 per cent success, v. Kries reports no success, Adler (Münich,) 61 per cent and Eversmann 100 per cent. The author conducted the experiment on forty-four women during the past year with 75 per cent success. The indications for medical intervention in the birth process at the ter-

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...mination of pregnancy are: 1. A medical indication, infection. 2. A social indication, shortening of the duration of the process. The advantages of the method are: 1. Total harmlessness for the mother. 2. Decrease in the length of the labor process. 3. The process is also entirely harmless for the child. 4. The afterbirth and hemorrhage after parturition have never been observed by the author.

On the other hand it is emphasized that medical intervention in the birth process is suitable only to be carried on in the clinic, and not in the practice, for one can not give to a midwife such variable remedies as the pituitary preparations. Under the accurate control of a physician, however, the Stein process is entirely without harm to either mother or child. The necessity for giving many injections is to be noted as an unpleasant circumstance, for many women have an aversion to the needle.

Diabetes and Pregnancy, Particularly concerning the Hormonal Relationship between Mother and Child. — Ernst Holzbach. (*Zentr. Gynäkol.*, **53** : 641, 1929.)

Casuistic contribution: A female diabetic who had cohabited for a long time and only first conceived after she had been treated with insulin and was sugar-free. Henceforth, one may be sure that more than the present 5 per cent of diabetic women will become pregnant if a greater number are treated with insulin. Many women are rendered entirely amenorrheic by diabetes, whereas in others after monthly amenorrhea menstruation is again instituted only after long treatment with insulin. The patients observed by the author were as good as sugar-free until the termination of pregnancy. Pregnancy also had a happy outcome in cases of disorders of metabolism. On the first day after parturition there again occurred a pronounced hyperglycemia in the mother.

Continued Investigations concerning the Influence of Insulin on the Respiratory Metabolism. — Cai Holten. (*Bibliothek for Laeger*, **121** : 49, 1929.)

The respiratory quotient rises in normal individuals after the injection of insulin, doubly as high as in diabetics. Concerning blood sugar the result is contrary, and the blood sugar is greater in diabetics than in normal individuals. Heat production increases in normal individuals after injection of insulin exactly as it does in those who have not received insulin. In normal persons insulin effects no changes in heat production, whereas it appears to cause a decrease in production of heat.

Parallel with the rise of CO_2 and heat production in normal individuals, the amount of ventilation increases about 16 per cent.

The respiratory quotient of diabetics after 12 to 14 hours following insulin injection is evidently higher than the existing process of oxidation accords and it is on the basis of formation of fat from carbohydrate. This synthesis ceases after administration of insulin. The drop in energy requirement which insulin seems to cause in diabetics is directly connected with the synthesis, since in this way a loss of energy is effected.

Genital Hemorrhages in Young Girls. — Kermauner. (*Wien. klin. Wochenschr.*, **42** : 297, 1929.)

Of the remedies for stopping hemorrhages, Kermauner prefers to give pituitary preparations besides the old medicaments. In pronounced hypoplasia ovarian preparations are also to be given, but only the best and most effective, and these only for a short time, so as to avoid an eventual too strong reaction.

On the Action of Several Amines. — H. W. Knipping and J. Steiger. (*Zeitschr. ges. exp. Med.*, **64** : 594, 1929.)

Several substances, such as adrenalin, acetylcholin, histamin, thyroxin, atropin, pilocarpin and others, were tested in general with regard to their effect on energy maintenance. The experimental animals were rats, rabbits and dogs. The chemical substances mentioned are related to one another in their identity with the group of amines. Thyroxin and histamin appeared particularly active, and also adrenalin with limitations. The action of adrenalin given *per os* fails, and in the case of thyroxin is very uncertain. In the case of thyroxin, besides a slight demonstrable action with other dosage, there occurs a specific cumulative action, which is not to be seen in other substances. Daily administration of thyroid gland combined with 0.0001 gm. organic iodin for a month produced a strong rise in metabolism, culminating in a maximum in a few weeks.

Increase of oxidation by means of adrenalin is not so great as one would expect from the

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general findings, while the rise of almost the whole process is dependent upon great muscular unrest. In contrast to the other total oxidizing, energy-increasing substances, in the adrenalin test, no relief from sleep was to be derived.

With coincident administration of adrenalin and histamin, instead of the expected rise in metabolic activity, there was found a great intensification with greater unrest of the animal. It is noteworthy that the secondary action of increased basal metabolism is much greater than with histamin and adrenalin alone.

Acetylcholin in suitable dilution arouses the parasympathetic nerves and the organs innervated by them. In the author's experiments the effect of 2 mg. acetylcholin chloride was slight. The action of thyroxin is basically different from that of other substances in that in acute tests it is slight, and in contrast, with longer administration, a sluggish action occurs. At best the metabolism can in general be increased by means of increased thyroidin dosage in 40 per cent of normal individuals, without incurring any noteworthy secondary effect. The same holds true in thyroxin experiments. The activity of thyroxin which is less when administered orally than when given parenterally is certainly to be traced to a destruction in the intestinal canal and is important practically if one considers that with natural thyroid gland substance given *per os* the same effects are obtainable with parenteral administration as with oral. Hence one would be bound to thyroxin injection.

Studies on the Physiology of Hunger Activity in the Digestive Apparatus. I. Contribution. Concerning the Kind of Hunger Movements of the Digestive Apparatus in Experimental Hyperthyrosis.

With persistent feeding of thyroid gland there was observed: 1. A permanent increase of hyperthyroid disturbances in the hunger movements of the intestine, which is apparently dependent upon a functional accumulation of thyroxin. 2. After 1 month feeding with thyroid gland — a continuous after-effect (in the course of 10 months) which induced an intermittent reappearance of typical hyperthyroid disturbances of the peristaltic action in hunger. 3. The two-fold character of the peristaltic action of the intestine of the dog in hyperthyrosis — namely excitation and depression — rests upon various functional adjustments of the parasympathetic section of the vegetative nervous system in the digestive apparatus. 4. The effect of thyroxin on the activity of the digestive apparatus during hunger in experimental hyperthyrosis permits the assumption that the functional condition of the thyroid gland plays an essential role in the mechanism of peristaltic action in the digestive apparatus during hunger.

Studies on the Physiology of Hunger Activity in the Digestive Apparatus. III. Contribution. Concerning the Influence of Cholin on the Hunger Movements of the Intestine. — Alexander Kratinoff. (*Zeitschr. ges. exp. Med.*, 64 : 404, 1929.)

The effect of cholin on the hunger movements of the intestine of the dog was studied. With intravenous injection during hunger it was shown that cholin exercises a periodic contraction of the already instituted movements; in subsequent movements cholin increases the amplitude and raises the tonus. The subsequent contractions of the intestine as isolated and denervated by Heidenhain were greatly increased by means of cholin. In agreement with the data of Le Heux and other authors, and on the basis of experiments conducted by himself, this author considers the premise to be quite correct, that cholin is to be regarded as a hormone of peristaltic action of the intestine.

Concerning the Daily Fluctuation of Adrenalin Effect in Human Beings. — Martha Lanwer-deHaan. (*Zeitschr. ges. exp. Med.*, 64 : 534, 1929.)

In healthy and diseased persons there was found a significant daily fluctuation of the reactivity to subcutaneously administered adrenalin. The adrenalin injection entered more rapidly in the afternoon than in the morning; the eruption was in general stronger in the morning hours than in the afternoon or evening. The lowest place of appearance seemed favored by the relatively stronger reaction. By means of this daily variation which was also observed in pulse, blood pressure, leucocyte count, infiltration and general reaction, the sensitivity of human beings for adrenalin is differentiated from sensitivity to all other chemical substances up to the present time.

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Concerning Hypertrophy in Pregnancy. — Hermann Knaus. (*Münch. med. Wochenschr.*, **76** : 404, 1929.)

On the basis of clinical investigations Halban presents the opinion that there must be, above all a hormone or a ferment of the placenta which limits the hypertrophy of the musculature of the uterus in pregnancy.

On the basis of biological investigations the author comes to the conclusion that the corpus luteum acts to further the development of the mucous membrane of the uterus while the function of the endometrium has an inhibiting effect, and indeed is influenced by the interrupted activity of the pituitary extract. On the other hand the placenta provides hormonally for the hypertrophy of the uterine musculature.

What Medical Therapy Is to Be Instituted in Cases of Melancholic Depression. — Kogerer. (*Mitt. Volksgesundheits.*, No. 3, 99, 1929.)

Upon consideration of the doubtless ever-present participation of the vegetative and endocrine systems, in each case a hormone therapy is to be essayed, either with any one of the reliable thyroid gland preparations if there is no contraindication (vagotonic symptom) or, on the other hand an energetic sex gland treatment is indicated.

Diseases of the Central Nervous System and Digestive Tract. — Alexander Pilcz. (*Wien. med. Wochenschr.*, **79** : 267, 1929.)

Kogerer gave insulin injections in five cases of tabes with intestinal crises, for example, on the first day, 5, from the second day on, daily, until one day after the cessation of the symptoms, 8 clinical units subcutaneously; hypoglycemic shock was never observed. The usual desire for sugar ½ hour after the injection could always be satisfied. It was possible often to abort the symptoms and to lengthen the pain-free intervals. Kogerer rightly brought out the advantage of the harmlessness of this therapeutic method of insulin injections. In a series of investigations on thirty cases of tabes with pronounced painful symptoms, of whom twelve had gastric crises, Kogerer and Halpern determined the blood sugar content and found it more or less increased (105 to 135 mg. per cent) while in sixteen cases of tabes without notable sensible secretory stimulation symptoms, the blood sugar content hovered between 90 to 116 mg. per cent.

Bolten summarized Quincke's disease as well as colica mucosa (enteritis membranacea) and also epilepsy, asthma, etc., under the classification of exudative paroxysms and recommends the administration of hormone, namely preparations for accelerating the endocrine glands (thyroid glands, adrenalin).

Consideration of the Treatment of Anemia with Liver. — N. G. Lupu and R. Brauner. (*Bull. et mem. Soc. med. hop. Bucarest et Soc. sc. med. Cluj*, **11** : 4, 1929.)

Successive description of six cases of anemia of varied etiology, which were all treated with roast liver, with good results. Patients who could not tolerate liver in this form could take it prepared according to the American method, in puree form or as orangeade. If the treatment is intercepted the symptoms of anemia again appear. Good results can always be obtained with liver treatment if the bone marrow is capable of regeneration. In one case of malarial splenomegaly good results were obtained; in one case of malarial cirrhosis with anemia the therapy was without success.

Studies on the Action of the Female Sex Hormone in Parabiosis Experiment. — Mahnert. (*Krankheitsforschung*, **7** : 79, 1929.)

The author's investigations present the fact that the female sex hormone which circulates in the body of one animal passes over to the partner in the case of successful parabiotic union of two animals, for there is shown in the uterus and its sheath the direct effect characteristic of ovarian hormone. The hypothesis for the success of the method is based exclusively on the treatment of ovariectomized animals.

The Endocrine Glands and Methods of Rejuvenation. — P. Niehans. (*Schweiz. med. Wochenschr.*, **59** : 255, 1929.)

Each organotherapeutic method, that is, method of treatment with gland extracts, is based upon the assumption of the absence of zoological specificity of the hormone, *i. e.* on the implication that the glands concerned in human beings and those in animals have the same function, to secrete the same kind of substance and to produce the same hor-

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mone which is constant for each given gland. The internal secretion of the gland of an ape, of a dog, of a sheep, etc. is identical with the secretion of the corresponding gland in the human being. The results obtained with industrially prepared organ substances are often only slight and insignificant if they are not given throughout the life of the patient, often several times daily. How then shall we administer by oral route a desiccated, pulverized gland, obtained by incalculable chemical and other processes, whose content of active substance is in no way certain, if it is possible to transplant a fresh living gland with the temperature of the animal body, under aseptic precautions.

The author reported concerning his own successful transplantation of various glands in various disease conditions as well as in children and in old people. The mortality from operation is zero.

Concerning the Cachexia of Cancer and the Manner of Combating It. — Pal. (*Wien. klin. Wochenschr.*, **42** : 321, 1929.)

The struggle against cachexia is an important factor. Cachexia is perceived as a symptom of endocrine insufficiency to which is ascribed the interrelationship of various glands such as the suprarenal cortex, the spleen, the sex glands. Stephan derived an extract from the suprarenal cortex which he called "Nerihormon." This hormone stimulates the formation of erythrocytes when given by subcutaneous injection.

The author came to the following conclusions:

In the bone marrow of the cancer cachexia patient it is possible to cause a regeneration of red blood corpuscles by certain substances of a series of biological amines, and therewith to improve the condition of the patient. Of the injectible preparations of the present time Pal found that the suprarenal cortex extract is effective. Histamin, because of its toxic reaction in subcutaneous administration is not valuable. Considering the duration of treatment, substances which can be administered orally are most satisfactory. Concerning liver, there are data given in the literature which indicate that liver therapy had no effect on cachexia of cancer (Seyfarth and others). In several cases of anemic cachexia — and also in carcinoma — the author himself has observed recovery after liver therapy as well as after liver extract treatment. It is true that not every case reacts. The path of recovery lies through the bone marrow.

On a Case of Tetany Due to Hypofunction of the Parathyroids. Good Results Obtained with Collip's Parathormone. — C. J. Parhon. (*Bull. et mém. Soc. méd. hôp. Bucarest et Soc. sc. méd. Cluj*, **11** : 1, 1929.)

A 40 year old woman suffered for 15 months with spastic symptoms which upon investigation proved to be manifestations of tetany. This was associated with great decrease of the calcium content of the blood. The patient received as treatment 20 units, subcutaneously, daily, of Collip's Parathormone. The tetany symptoms receded; a blood test showed hypercalcemia. With interruption of the injections the symptoms reappeared.

The Collip extract was prepared from the parathyroid glands of animals by means of hydrolysis with diluted acid salt solution. Collip, Liser and Schaphardson, Snelle and Habein have obtained good results in human beings.

The Regulation of Carbohydrate Metabolism. The Excretion of Insulin by the Kidneys and Related Parts. — Alexander Partos. (*Pflügers Arch. ges. Physiol.*, **221** : 562, 1929.)

The author obtained insulin from the urine with a slight modification of the Collip method. The extract contained besides the insulin, chiefly creatinin.

It was demonstrated that insulin is a normal constituent of human as well as rabbit urine. In fasting rabbits there is no insulin in the urine.

In a condition of hyperglycemia the urine excreted contains no insulin; as soon as the blood pressure begins to decrease, however, insulin appears in the urine.

In human as well as in experimental pancreatic diabetes no insulin can be demonstrated in the urine.

Continuation of Researches on the Heart Hormone. The Active Constituent of the Frog Heart Hormone of Haberlandt. — R. Rigler. (*Pflügers Arch. ges. Physiol.*, **221** : 509, 1929.)

The hormone, derived according to the latest contributions of Haberlandt, in this case was not the hormone of the frog heart, but the bull, and presented, not pure sub-

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stance, but rather an extract, with which excitation of the heart was possible also in warm blooded animals, as stated; in addition it should lower the blood pressure by dilatation of the blood vessels. According to the author's experiments the frog heart hormone of Haberlandt is endowed for its effect, with two different substances. The one alters the force and the other the rhythm of the beat. Reduction by burning to ashes brings out the inotropic but not the chronotropic action of the frog heart hormone.

The chronotropically active constituent of the frog heart hormone is potassium, the inotropically active portion corresponds to the Clark substance.

Under the limitations of the author's experiments the potassium threshold of the frog heart represents a Ringer solution with 165 mg. KCl per liter.

The Extraction of the Female Sex Hormone and Information concerning Folliculin Therapy. — Serdukoff. (*Gynécol. et Obstét.*, **19** : 39, 1929.)

The follicle has the following significance for the female organism.

It acts 1, as a generative agent; 2, as a protection for the uterus; 3, as an influence on the periodicity of function of the female organism; 4, for sensitization of the mucous membrane of the uterus for implantation of ovum; 5, for strengthening the heart contraction (Beloff); 6, liquor folliculi has a hemostatic effect; 7, as an influence on the secondary sex characteristics and on bone growth; 8, as sympathicotropic influence; 9, for sensitization of the uterus muscle for contraction; 10, for regulatory increase of secretion of isolated parts of the sex glands. Folliculin therapy is of three kinds. 1, in the form of fresh liquor folliculi from the ovary of the hog, 2, as an oily solution, and 3, as a watery solution. Fresh liquor folliculi, in general, forms no coagula, not even after 24 to 36 hours. The oily solution is an emulsion in which there are amorphs after the contraction of the albumin of the folliculin. The watery, albuminous solution is slightly opalescent; it can be put up in ampoules, but loses some of its strength after long storage.

The author conducted folliculin treatment in 125 cases of women between the 14th and the 50th years, especially for headaches, vertigo, congestion, vomiting, migraine, general weakness, irritability and fatigue.

The therapy is applied in the following cases: In cases of atrophy of the uterus with hypo-ovarianism, in cases of congenital aplasia of the uterus, in post-operative atrophy of the uterus with obesity, in the menopause, in habitual abortion, in meno-metrorrhagias of puberty, in malposition of the uterus, in adiposogenital dystrophy and in acute inflammatory processes. The therapy was confined to folliculin administration in 75% of the cases, in 25% calcium was also injected intravenously.

The results were satisfactory with regard to objective findings as well as subjective. Blood tests 24 hours after the commencement of treatment also confirmed this. The lymphocyte count rose about 10 to 20 per cent, that of the eosinophils about 2 to 4 per cent; further a shift to the left (Schilling) was observed. Blood pressure showed an increase 2 to 3 hours after the folliculin injection. The blood calcium content remained unchanged. The secretion of the vagina showed an increase of epithelial cells and an alkaline reaction, which lasted about 24 hours. The general findings and the constitution of the patients were very much improved after 2 weeks of treatment.

The Utilization of Spleen Contraction by Means of Adrenalin in Spleen Operations. — P. E. Weil and R. Grécoire. (*Presse méd.*, **37** : 326, 1929.)

For the purpose of obtaining contractions of the spleen in spleen operations the authors injected adrenalin. The following results were thus obtained in three cases of primary splenomegaly: Once the spleen was rendered entirely bloodless, in the second case it contained only one-tenth of its former blood supply and in the third case the evacuating action was quite weak and gave no measurable result. Usually this organ contained one-fourth or one-fifth more blood than its own weight.

The injection of 1 mg. of adrenalin should be made $\frac{1}{4}$ hour before splenectomy. It is possible to predetermine to a certain degree the effect of the adrenalin injection in a special case if, on the day preceding the operation a test injection is made and the change in spleen volume obtained by means of diagrams. The adrenalin injection spares the patient the loss of a large quantity of blood; in itself it is harmless and lessens the severity of the secondary consequences.

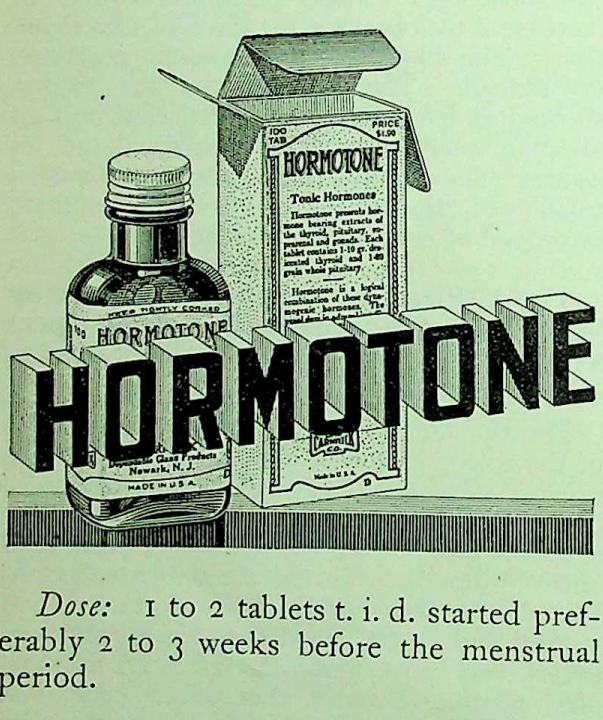
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Action of Hormotone Curative, Not Palliative

The therapeutic effect of Hormotone in dysmenorrhea is that of restoring a disturbed endocrine menstrual mechanism to normal. It is not a palliative effect. The results obtained at the Woman's Hospital, Soho Square, represent a cross-section of the experience in general medicine.

"Fifty cases were treated by organotherapy . . . . The majority were treated with Hormotone as follows . . . 46 of the cases so treated were relieved."



Dose: 1 to 2 tablets t. i. d. started preferably 2 to 3 weeks before the menstrual period.

Bottles of 50 and 100 Tablets

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NEWARK, N. J.

The Therapeutic Application of Acetylcholin. — M. Villaret and L. Justin-Besançon. (*Lancet*, **216** : 493, 1929.)

The vagal activity of acetylcholin, which has been determined by Henri Fredericq, makes it clear that this substance is considered by several physiologists as a vagal hormone. Acetylcholin effects an excitation of the smooth musculature and in extraordinarily strong dilutions causes peristaltic activity in the isolated intestine. Acetylcholin is given either subcutaneously or intramuscularly; intravenous injections are dangerous, oral administration seems to have no effect. Besides its influence on the arterial blood pressure, its action on the heart, muscle and blood is noteworthy. It is given therapeutically on the basis of the fact that its vasodilatatory property is localized in the arteries and arterioles and that it possesses a similar influence on the vago-sympathetic system. The author, as well as others, gives acetylcholin in Raynaud's symptom complex, gangrene originally from arteritis and in similar disturbances. In diabetic arteritis the administration of acetylcholin plus insulin is more effective than insulin alone. Kalt contributes a very interesting case of thrombosis of the retinal artery with blindness which presented extensive improvement from the time of the first injection. The author has observed that the profuse sweats in tuberculosis patients are improved in a remarkably favorable way by means of treatment with acetylcholin.

Experimental Studies on the Functional Significance of the Theca Interna Cells. — Axel Westman. (*Acta obstet. et gynecol. scand.*, **8** : 290, 1929.)

The author conducted experiments on rabbits in order to test whether the cells of the theca interna have the capacity for producing hormone which is the analogue of that derived from the follicle cells. The experiments provide definite basis for the assumption that an apparently swift atrophy occurs in the cells of the theca interna when the follicle is divested of its granular membrane and thereby inhibited from forming corpus luteum. At any rate the results obtained indicate the fact that the theca cells in the wall of a mature follicle are not unable to produce the characteristic reaction of corpus luteum in the uterus, after the follicle has been deprived of its granular membrane. The author raises

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the question whether various hormones which effect a reaction in the vagina, such as changes in the mucous membrane, will be produced in the ovary.

Action of the Anterior Lobe of the Pituitary on the Development of the Genital Tract. — Watrin. (*Bull. soc. d'obstet. et de gynecol. de Paris*, No. 6, 433, 1929.)

The author investigated for 1½ years the possibilities of pituitary activity on guinea pigs not yet sexually mature. He comes to the conclusion that transplantation is a more reliable and scientific form of test than injection of pituitary extract and that the ensuing activity is more of a quantitative than of a qualitative nature. Further, the author believes that the changes in the uterus and in the vagina are definitely connected with the ovary.

Action of the Anterior Lobe of the Pituitary on the Ovary Treated with X-Rays. — A. Walter. (*Endokrinologie*, 4 : Part 1, 1929.)

Two months after x-ray therapy of the ovary with dosage considerably above that causing sterility, a total disappearance of follicles is obtained, then there is found on all sides, theca cells full of lutein. Such an ovary is able, however, to sustain the rut cycle, usually a permanent estrus follows. For the creation of estrus then an ovum or fresh corpus luteum is not necessary, but the theca cells must be the hormone agent or generator. When implanted with anterior lobe of the pituitary gland the ovary of very young mice which have been treated with x-ray only acts during the first week (provided not all the ova have been destroyed) in the manner similar to that of follicle maturity and the formation of corpus lutea atretica. Later, when the ovary consists only of lutein tissue, it reacts no more to implantation.

Concerning the Combined Action of Quinine and Pituitary Gland on the Puerperal Uterus of the Living Cat. — K. Schübel. (*Klin. Wochenschr.*, 8 : 1555, 1929.)

Quinine is a general cell toxin which arrests the anabolistic as well as the catabolistic processes in the cell. The point of attack must be sought for in the enzyme. The diversiform activity and applicability of quinine and its derivatives must be attributed to this influence of the cell. Of particular interest is the manner of the secreting and acting on the uterus. After per os administration at the most 3 per cent appears in the blood, after 24 hours the quinine is secreted. After intravenous and intramuscular injections two-thirds of the quinine is destroyed in the organism, the rest is retrieved after 8 hours. Liver, kidneys and suprarenals must hold back a small amount of the quinine for a long time. Doubtless, also the puerperal uterus retains quinine for a long time, for 2-5 days after injection labor pains were observed. For seventy years quinine has been administered to bring on labor pains with variable results. "Quinine is a capricious medication." In numerous experiments on puerperal cats it could be shown that 25, 50, 100 and 200 mg. of quinine injected intramuscularly, paralyzes the uterus until, either by secretion or destruction of alkaloids, the optimum of concentration is attained in the organism; then severe pains ensue. If one inject 1 mg./kg. quinine, after 1-2 hour, uterus contraction occurs. After intravenous injection of ½ mg. quinine per cat, labor pains are observed. Quinine is a toxin dependent on time. One must indeed agree that up to the present too much quinine has been administered to aid labor pains in human beings (repeatedly 0.3, 0.75-1.0 gm.!) 60 mg. is sufficient for muscular injection. Quinine sensitizes the uterus against mechanical and chemical influences.

On the Pathogenesis and Therapy of Psoriasis. — Erwin Pulay. (*Deut. med. Wochenschr.*, **55** : 1175, July 12, 1929.)

The works concerned with the question of the pathogenesis of psoriasis after endocrine impetus are numerous. An average type of constitution with definite administration of incretion substance did not work out well. Greater interest would be attached to the function of the thyroid gland except that an individual standpoint is incurred. The Abderhalden reaction on the pancreas, suprarenals, thyroid gland, liver and spleen gave diverging results. The rôle of the generative glands is also particularly discussed. Here, too, there is no regularity. Clinical observations often show either exacerbation or amelioration at the time of the menopause or at puberty, etc.

"In order to approach the problem with some sort of exact method, I made systematic investigations on metabolism. On the

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whole my observations were presented in three groups: those related to the hypothesis of depressed function (indication for thyroid gland therapy), those related to the hypothesis of increased function (contraindication of thyroid gland therapy) and those related to the hypothesis of depressed function and intense specific-dynamic albumin effect."

The divergent results must be referred to another gland incretion.

Cases of specific-dynamic albumin reaction permit the consideration of the possibility of disturbance of the pituitary gland. Yet, it could not be presumed that there was any causal relationship on this score. Upon reconsideration of the observations the fact becomes evident that in no case of psoriasis is there a normal process of metabolism. The endocrine disturbance seems to be closely connected with it. Upon application of the Abderhalden reaction this assumption seems to be further strengthened. In the first place the pancreas was exhausted.

The intense decomposition of the pancreas bears a definite relation to the voluminous information on the activity of insulin in psoriasis, and further, it is of particular interest in view of the very evident hyperglycemia, and finally in the frequent appearance of pancreatic disturbance in the intestines of psoriasis patients. From this viewpoint the foregoing, apparently heterogeneous conclusion derived a definite importance on account of this one fundamental distinction. The hormone correlation which exists between the pancreas, on the one hand, and the thyroid and pituitary on the other, suggested the consideration of metabolism. The functional adjustment in the pancreas in one case leads to rise and in another to intensification of the basal metabolism. The fact of the extensive interrelationship of secretion and incretion of the pancreas must be held fast. The pathogenesis of psoriasis points straight to a disturbed condition of the ferment.

Liver Therapy of Anemia in Nurslings and Young Children. — Jerachmiel Ligum. (*Monatsschr. Kinderheilk.*, **43** : No. 6, 1929.)

In accordance with observations of the Basler Children's Clinic, in various anemic conditions, even in the anemia of premature birth, essential results were obtained with liver therapy. The result of treatment with liver is therefore not only confined to the anemia of adults. Liver therapy has, however, the disadvantage that in many children it meets with aversion and occasionally therefore incurs failure, even with careful dosage; this is particularly true in the case of prematurely born children. Either liver juice obtained from fresh calves' liver or calves' liver cooked in water and then finely pulverized and mixed with the midday meal was given. We began with very small doses, in nurslings and prematurely born children the liver juice was administered in drops (20-40 drops three times daily). Results were obtained at first with large doses (20-80 gm. liver substance daily). The optimal amount was 15 gm. of liver substance for a kilogram of body weight, per day. This amount had scarcely any effect on the children. Good results were also obtained with Merck's liver powder. Dosage began with 1 gm. daily and was increased to 25 gm. The anemia decreased in about 4 weeks with liver treatment. The well established iron therapy must not be surrendered, however, to the liver therapy.

Labor and the Puerperal State. — W. Lahm. (*Geburtsh. Rundschau Jahersk. ärzil. Fortb.*, **20** : 12, 1929.)

Hatzki reports from the Obstetrics Institute (Stroeder) in Hamburg concerning the results of the injection of pituitary substances in labor. Pituitary gives successful results in about 30 per cent and failure in about 60 per cent. One can thus attempt the injection in cases of premature birth only if no danger ensues for mother or child from the unsuccessful result; with very premature children the test fails entirely. The thymus extract obtained from von Temesvary was tested in numerous experiments and in general a favorable criticism was obtained.

The Therapy of Allergic Diseases. — van Leeuwen and Storm. (*Fortschr. Therap.*, **5** : 41, Jan. 25, 1929.)

The best symptomatic medium for the prevention or suppression of cases to be treated is doubtless adrenalin. It acts promptly and almost never fails. Besides, in all cases refractory to adrenalin all other asthma remedies, with the exception of morphine, fail. It is further to be noted that there is no inuring to adrenalin and no adrenalemia. Naturally, abuse arises, but the author observed this only in desperate cases, in which there was merely choice

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between the question of abuse of adrenalin or abuse of opium derivatives. The author maintains that in the treatment of all allergics it is desirable to supplement the attacks with adrenalin. In cases of long existing asthma with functional emphysema and ultimately with bronchitis, the adrenalin injection is to be considered as direct causal treatment.

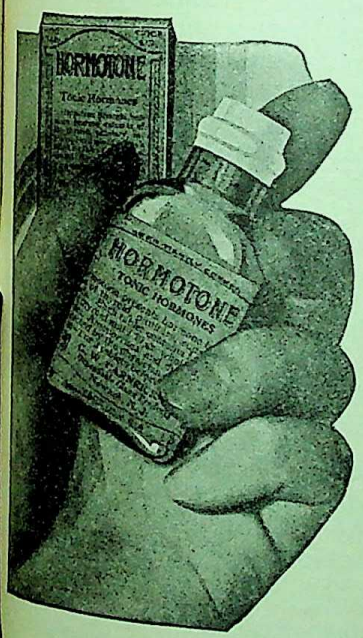
Cell Formers and Cell Forms of the Blood. II. Experimental Studies on Blood Formers after Adrenalin and Thyroxin Injections. — W. Stockinger. (*Zeitschr. ges. exp. Med.*, **65** : 52, 1929.)

The action of the both hormones, adrenalin and thyroxin was studied by the author, and from this less stress was placed upon the numerous changes of the white blood corpuscles than on the morphologic peculiarities of the cell forms under the influence of the both hormones.

A schematic report on the action of both hormones on the formation of the blood was not possible on account of discrepancy in the reaction. In myxedema the anticipated increase in cells following adrenalin administration fails. The process of increase of leucocytes after adrenalin and thyroxin takes place by means of the appearance of new basophilic cell elements. Adrenalin and thyroxin are both capable of initiating the transposition of cells for oxidative metabolism or for augmenting it.

Ephedralin, a Combination Product from Ephetonin and Adrenalin (Paranephrin). — H. Kreitmair and M. Leffkowitz. (*Deut. med. Wochenschr.*, **55** : 480, 1929.)

Blood pressure test shows that the prompt, brief action of adrenalin and the slow lingering action of ephetonin can be combined for an index of efficacy. And in cases of asthma,



Hormotone is theoretically a specific type of therapy in dysmenorrhea, for it contains those endocrine substances elaborated by the body for the specific control of menstruation.

It is practically successful in medical practice as demonstrated by over 20 years of widespread use in the profession.

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in the struggle for breath in chronic bronchitis and in emphysema, the pre-eminence of the combination and the prompt and long persisting effect finds clinical acceptance.

Further Application of Exsanguinated Suprarenals. — E. Borschers. (*Der Chirurg*, **1** : 389, 1929.)

The author shows by massive supporting evidence that extensive infiltration of the soft parts results with the use of adrenalin and also in narcosis during operations; 30 to 40 drops of suprarenal stock solution may be added when applying 200-400-800 NaCl solutions to the infiltration of the soft parts. By this procedure many operations may be rendered bloodless.

Insulin-Like Substances from Bact. Coli and Anthrax Bacilli. — S. Breüer. (*Münch. med. Wochenschr.*, **76** : 741, 1929.)

The author has previously reported in 1926 that culture filtrates of *Bact. coli* injected into rabbits intravenously in doses of 4-6 cc., induced a sluggish though eventual lowering of blood sugar. Later the author has investigated special cultures of anthrax bacillus for glucokinin formation and has found that, estimated on similar quantities of culture, the yield of glucokinin, in contrast to that of *coli* and *subtilis* is at least four times greater. The simple heated shaking autolysate of the bacteria shows a decreased blood sugar action.

Concerning the Attenuation of the Toxicity of Adrenalin by the Hypotensive Substance of the Pancreas. — Vaquez, P. Gley and Kisthinios. (*Paris méd.*, **19** : 445, 1929.)

The authors present the fact that the hypotensive substance of the pancreas, which is different from insulin, possesses the capacity, when applied intravenously, to lower the toxic action of adrenalin in rabbits. It seems that this substance protects the animals from acute edema in the lungs induced by adrenalization.

Insulin Treatment of Hyperthyroidism. — Coffin and J. S. Losse. (*Bruxelles méd.*, **9** : 668, 1929.)

The results obtained by the author with insulin treatment are as remarkable as any could be from patients in whom every other therapy had failed. On the other hand, the insulin therapy was followed by years of improvement. Daily insulin injections of [illegible] units effect a definite lowering of basal metabolism and a coincident increase in body weight, quieting of the pulse and extensive quiescence of the psychic state of the patient.

Discourses on the Disturbances of Arterial Blood Pressure. — C. Achard. (*Progrès méd.*, **57** : 637, 1929.)

Medical therapy of arterial hypotension is primarily concerned with the administration of adrenalin and for this purpose, adrenalin was diluted with sufficiently large amounts of common salt solution and injected subcutaneously. In very severe cases intravenous injection is to be preferred. The arterial hypotension of tuberculosis is likewise to be offset with adrenalin, but the treatment must be stopped at once if the sputum gives the least evidence of filamentous blood particles.

The Use of Acetylcholin in the Clinic and for Therapy. — Maurice Villaret. (*Monde méd.*, **39** : 459, 1929.)

As conclusions of three instructive case histories the author presents evidence of the diagnostic and therapeutic value of acetylcholin. He reviews his case histories, their peculiarities and the method of their treatment. Acetylcholin decreases the blood pressure by means of its action on the peripheral arterioles. Hence it can be administered advantageously in cases of arteritis obliterans. Twenty cg. are given intramuscularly, mornings and evenings. In cases of arterial hypertension 10-20 cg. are given. In ophthalmology, acetylcholin is given to offset spasms of the retinal blood vessels with blindness. Finally it is used with success in a few cases of hemiplagic apoplectic seizure.

The Presence of the Hormone of the Anterior Lobe of the Pituitary in the Urine. The Zondek-Aschheim Pregnancy Reaction. — R. Brühl. (*Münch. med. Wochenschr.*, **76** : 818, 1929.)

The so-called Reaction 1 of Zondek and Aschheim gives evidence of at least two hormones from the anterior lobe of the pituitary gland. It is agreed that the existence of both these hormones, the one inducing the growth and maturation of the follicle and the other resulting in luteinization, is necessary for the undisturbed process of the female cycle, so that with the transference of one of

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these hormones, or with its deficiency, disturbances can arise, such as are common in the climacterium.

Extended Application of Suprarenin Anemia. — E. Borschers. (*Der Chirurg*, **1** : 389, 1929.)

Suprarenin can accomplish much more than has been recognized up to the present, and the author is convinced after a year of experimental investigation and test in the operating room, that this medium can in no wise be substituted. There are only a few instances in which — though often only slight — a need for bloodless condition induced by suprarenin is not to be desired and the various possibilities of application are surprising if, preceding each operation, one asks oneself if it is not necessary for the patient and agreeable for the operator to operate bloodlessly. The author has performed bloodless operations in prostatectomy, large umbilical hernia and scar rupture, ureterotomy, resections of the tongue and the floor of the mouth and the Whitehead operation for hemorrhoids, without a single ligature, without loss of blood and without hemorrhage thereafter. Nephrectomy, radical operation of mammary cancer, resection of the bladder, operations on the spinal cord, in the region of the hip joint, can be operated upon with relatively few ligatures by this method. Extensive operations in the thorax lose some of their dreadful aspect if aspirations are applied in and around the flaps of the soft parts. The author is definitely convinced that the so-called operation shock in severe cases will be greatly reduced if not suppressed, if the loss of blood is checked or decreased. The application of suprarenin is also very useful in the case of children.

In inflammatory processes suprarenin can only be valuable if there is a case of circumscribed disease condition, which can be surrounded by a suprarenin coating in healthy persons.

The fact can not be contested that checking of the blood flow and shortening the operation (by the absence or decrease of ligatures) often becomes a life-saving factor.

The Therapy of Epileptiform Symptom Complexes. — Max de Crinis. (*Mitt. Volksgesundheits.*, No. 4, 101, 1929.)

The study of metabolism and internal secretion has been a stimulus to the treatment of epilepsy by means of organ preparations. Bolton has given fresh expressed juices of thyroid and parathyroid rectally, it is stated, with good results. The author has found thyroid tablets also effective in a few cases. These results with thyroid gland preparations will perhaps be intelligible, since in epileptics there is often present an aplasia of the thyroid gland.

Concerning the Modern Treatment of Rheumatism. — Ernst Freund. (*Mitt. Volksgesundheits.*, No. 4, 118, 1929.)

For medical therapy the hormone is mentioned. The most common to be administered are ovarian and thyroid gland preparations. Concerning the latter, emphasis must be placed on the fact that it possesses not only a hormonal action but also a pharmacological action, so that a conclusion as to the etiology can not be drawn from the therapeutic result.

Results of Acetylcholin Treatment of Lead Colic. — Laignel-Lavastine and Jean Fouquet. (*Progrès méd.*, 520, 1929.)

A 30 year old workman who suffered a sudden severe lead colic was treated with acetylcholin, whereupon the colic pains disappeared. Simultaneously obstipation vanished with the pains and abdominal retraction, arterial hypertension and vasoconstriction disappeared also.

Action of Acetylcholin on Glycemia. — M. Labbe, F. Nepveux and L. Justin-Besançon. (*Paris méd.*, **19** : 316, 1929.)

The injection of 20 cg. of acetylcholin fairly regularly causes a decrease of glycemia, which, however, incurs individual variations. This decrease can be intense and of long duration in healthy persons. In certain forms of diabetes and obesity it seems rather intense.

Concerning the Treatment of Coma Hepaticum, Especially with Regard to Injury to the Liver Parenchyma, in the Course of Gallstone Troubles. — G. E. Konjetzny. (*Zentr. Chir.*, **56** : 770, 1929.)

The author obtained favorable results in two cases of very severe cholemic condition with insulin-grape sugar treatment used by Umber and Richter, and he therefore held it obligatory, in similar cases, to test the effect of insulin-grape sugar treatment in each instance. (1000-2000 cc. of a 5 per cent solution of grape sugar per day, and to each 2.3

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gm. of grape sugar a unit of insulin.) The premise for the undertaking is generally the presence of some efficient liver parenchyma. The symptomatic value of grape sugar-insulin treatment in carcinoma of the liver is also emphasized. The painful symptoms which accompany this condition will be actively combated.

Pituitary and the Law of Puberty. — A. Lipschütz, H. Kallas, and R. Paez. (*Pflügers Arch. ges. Physiol.*, **221** : 695, 1929.)

The anterior lobe of the pituitary of castrated guinea pigs acts the same on the genital organs of infantile mouse as does normal pituitary. The action still occurs even after a year's castration on the part of the donor.

The uterus is also affected by the administration of pituitary of young or infantile animals.

In positive cases the effect in the ovary after administration of pituitary from either an adolescent or an infantile animal can be determined.

Likewise after the injection of pituitary of a 14 year old senile dog changes occurred in the uterus and ovary.

The report of Smith and Engle, that the anterior lobe of infantile animals secretes hormone and that that of old animals still produces it, is confirmed.

Concerning Several New Medicaments. — René Hazard. (*Bull. méd.*, **43** : 381, 1929.)

According to the latest experimental investigations it appears that actually there is agreement between natural thyroxin and synthetic thyroxin (identity) and that hyperthyroxination induced in animals of various sorts is the same as a condition of hyperthyroidinization. Thyroxin administered *per os* gives the same results with respect to appearance and duration as thyroid gland extract. One mg. of thyroxin is really about the same as 0.20 gr. thyroid gland extract.

Ovarian Hormone, Insulin and Carbohydrate Metabolism. — E. Kaufmann. (*Deut. med. Wochenschr.*, **55** : 650, 1929.)

The ovarian hormone affects carbohydrate metabolism in the exact opposite manner of insulin. On this basis are explained the sensitivity of children to insulin, the danger of hypoglycemia in diabetic puerpera, the slight decrease of carbohydrate metabolism in the ovarian cycle and in the process of pregnancy in diabetics.

The Therapy of Nephrosis with Liver Extracts. — L. Rohácek. (*Zentr. inn. Med.*, **50** : 337, 1929.)

By nephrosis the author understands the symptom of Volhard's genuine nephrosis, not the various sorts of "nephrotic complexes." In a patient with edema in whom the therapy with urea was unsuccessful, he first tried a therapy with kidney and liver extracts, based on the idea that in the kidney and liver there might be a regulatory substance which might have an effect on the assimilation of water and also on the metabolism of salt. First the patient received only renin injections, later alternating renin and hepatin injections (for 4 months). The symptoms of edema did not occur from the time of the hepatin injections. Likewise the hypercholesterinemia entirely disappeared. The author also investigated the effect of the therapy on other patients. In nephritis, and such cases, also, as nephrotic degeneration, the remedy did not have a lasting effect.

Regarding the hepatic activity in patients afflicted with liver diseases the author found that hepatin facilitates the removal of chlorides from the tissues into the blood. In atrophic cirrhosis the action of hepatin is only superficial and it is not possible to cure the cirrhosis with hepatin.

Pituitary and Genital. — J. Novak. (*Med. Klin.*, **25** : 643, 1929.)

The active substance which induces the changes in the ovary is contained in the anterior lobe of the pituitary, alike in infantile and senile animals. The action of the anterior lobe on the accessory sex characters is only possible if the sex glands are included, so that the pituitary is correctly considered as the initiator of sexual function. The active substance of the anterior lobe is water-soluble but not lipoid-soluble. It is not an albuminous substance, and is very sensitive to heat, acids and alkali. As mouse unit the amount used was that which brought about in 100 hours, in a mouse weighing 6.8 gm. the characteristic changes in the ovary, and initiated estrus. The rat is much more sensitive than the mouse. In pregnancy the pituitary produces much more hormone than formerly. This hormone is evident in the urine, in the placenta and in the blood in large quantities.

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The author was successful in bringing back the menses in a case of amenorrhea, but he emphasizes the disadvantages of dosage and the causal analysis of the disease symptoms. However, the hormone of the anterior lobe of the pituitary ought to be tested on genital hypoplasia and in premature involution. The reports of results in experiments on animals and human beings are vastly different from each other. There is no evidence of efficacy in childhood or in the climacterium, although the pituitary produces hormone in these periods, also. Further, the author hopes that the administration of the hormone of the pituitary will become as important as the administration of thyroid and insulin.

Investigations on the Hormonal Activity of the Anterior Lobe of the Pituitary of the Fetus in Animal Experimentation. — F. Schultz-Rhonhof and R. Niedenthal. (*Zentr. Gynäkol.*, 53 : 902, 1929.)

The authors implanted the pituitary of a human fetus in animals and three sexually mature castrated mice and eighteen infantile animals each were implanted with an entire pituitary. Two infantile mice were each implanted with two whole pituitaries.

From this it was seen that in none of the cases was the ovary entirely unaffected, although the changes were often only slight. Also in almost all the cases the secondary reaction of the vaginal orifice is evidence of the fact that the hormone of the anterior lobe of the pituitary must have expanded its action first in the ovary. The finding of the author settles the contested problem of whether hormone of the anterior lobe of the pituitary of human fetus produces the hormone stimulating ovulation, affirmatively. In tests with the anterior lobe of the pituitary of fetus cortex, it is evident that a production of the hormone influencing ovarian function is also present in the animal fetus.

Observations on the Fall in Temperature Directly after an Insulin Injection in Two Cases of Protracted Increase in Temperature. — A. Puech. (*J. practiciens*, 43 : 833, 1929.)

For the purpose of increasing the appetite and improving the general condition, an insulin injection was made in a patient who for more than a month had had a temperature between 38° and 39°, and in whom no basis could be found for the height of temperature. The temperature fell promptly to 37.5° and after 3 days a total recovery of the patient was obtained. Fifteen units of insulin were injected in another case in which, for ½ year the temperature stood between 37° and 38° and every therapeutic attempt had been unsuccessful. On the day immediately following the patient was free of fever and remained so. Though unable to explain the mechanism of recovery in these two cases, the author thinks that the matter was not one of entirely accidental occurrence.

Concerning the Mode of Action of the Thyroid Gland Hormone. — Weil, R. Landsberg and M. Landsberg. (*Biochem. Zeitschr.*, **207** : 186, 1929.)

The authors undertook investigations in order to study the processes involved, especially in the albumin metabolism of thyroxin, above all in the liver as the chief place of all metabolism, and have tested the influence of thyroxin on the autolysis of liver broth (guinea pigs). The autolytic process shows a synonymous increase of the mechanical destruction of tissue structure, independent of the pH of the medium, a slight increase also with substances other than thyroxin.

The point of view concerning change in water-salt metabolism under the influence of thyroxin is in accord with the theory of permeability of thyroxin activity. The wandering off of electrolytes from the tissues into the blood is certainly the primary process in the diuretic effect of thyroxin. Consequently, the thyroxin induces a better distribution of electrolytes. It is doubtful whether thyroxin calls forth increased tonus of the autonomous nervous system. The experiments of the authors show that thyroxin, in dilution to 1:400,000 quantitatively furthers the tissue autolysis by neutral reaction. As an outcome of this observation the authors sought to explain consistently the manifold metabolic effects of the hormone of the thyroid gland on a physico-chemical basis, that, since each stimulation induces further permeability of the plasma membrane, it is theoretically possible to increase or inhibit, simultaneously, by hormone or nerve, the identical or contrary effect on the cells.

The Heart Hormone. — Zuelzer. (*Med. Welt*, **3** : 511, 1929.)

The author reiterates that he doubts the hormone nature of the substance designated

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by Haberlandt as heart hormone. Haberlandt alone is responsible for the proof of the hormonal nature of his substance. This fact is all the more difficult to prove, as has been said at the Vienna Conference for Internal Medicine, for many chemical substances have the same effect on the frog heart as the heart substance of Haberlandt. Since the frog heart has no coronary arterial system, it is particularly inappropriate and unnecessary to draw conclusions concerning its reaction to the activity of a hormone. To this end convincing experiments on mammals must be undertaken.

Female Sex Hormones. Contribution to their Experimental Study. — F. G. Triviño. (*Med. Ibera*, **21** : 225, Sept. 17, 1927.)

The serum from pregnant women produces in infantile rats, that is, in rats with genital organs still immature, in addition to initiation of the estrous cycle, a marked increase in size of the uterus. The active substances proceeding from this serum are thermostabile, soluble in alcohol and apparently diffusible.

The content of these substances per cubic centimeter is 10 biological units and as site of their production the quantitative content of the ovary in these substances can not alone be taken into account. Probably the placenta and perhaps the uterine wall contribute to their production.

Clinic and Therapy of Arterial Hypertension. — J. Pal. (*Med. Klin.*, **24** : 160, 1928.)

Several authors have described a lasting blood pressure-lowering effect of certain liver extracts.

The author carefully tested various preparations of the type, clinically as well as experimentally, but without exception in all cases he had to record unsuccessful results with these preparations.

Concerning Liver Extract Treatment of Pernicious Anemia. — Seyderhelm and G. Opitz. (*Klin. Wochenschr.*, **7** : 205, 1928.)

Every speculation concerning the true nature of the active liver substance, in particular every discussion whether it is a question of a vitamin or a hitherto unknown hormone, must remain without purpose as long as it has not been possible to free the specific active principle of the organ and investigate it experimentally and biologically. In the following a report will be made concerning a liver fraction analogous to that prepared by Minot and Murphy with Cohn. Analysis of this extract gives: N: 7.8 per cent, P: 3.4 per cent, Fe in traces, S: 0.015 per cent, NaCl: 1.46 per cent, Alb. Peptone, Polypeptide: (+). As a rule the patient with pernicious anemia was given as much liver extract as corresponded to the amount of 400-500 grams of fresh liver, that is 7.5 grams of the desiccated substance and 80 grams of the fluid substance, that is, about 4 tablespoonfuls. The effect of the liver extract on pernicious anemia is effectively the same as is attained by administration of liver. It appears that later after attainment of the normal blood count one can go back to an amount of extract corresponding to 200 grams of fresh liver. It is remarkable that also after administration of liver extract in the majority of cases the change in subjective condition as well as in blood picture sets in already within the first week of treatment. Almost regularly an increase in leucocytes appeared simultaneous with the slow rise in hemoglobin and erythrocyte count. Instead of leucopenia with relative lymphocytosis and deficiency of eosinophil cells, an increase in neutrophil leucocytes appeared, for the most part accompanied by a rise in eosinophil cells. Moreover, in the majority of cases — very frequently even during the first week of liver extract therapy — occurred the retrogression of urobilinogen and urobilin as well as indican in the urine. In other cases, the improvement introduced by means of liver diet proceeded entirely similar upon transition to liver extract treatment. In three patients examination of the gastric juice following liver extract treatment showed the disappearance of colon bacilli always present in quantities before treatment. The demonstration of colon bacilli in the gastric juice in pernicious anemia is so regular a finding that diagnostic significance may be ascribed to it.

The reappearance of hydrochloric acid production of the stomach observed in one case of pernicious anemia following liver extract treatment was most striking. This single observation shows that with liver therapy actual lost functions in the sphere of the intestinal tract may be restored. With all precaution it should be declared that the observations made allow the possibility of a primary influence of liver extract on the intes-

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inal functions to appear disputable. Finally, it must also be mentioned that even in hypochrome "secondary" anemias, striking successful effects were observed with liver extract; of course, such cases in practice are treated as well with iron or arsenic. An eventually refractory course would justify a trial of the costly preparation — whether it be daily feeding of liver or liver extract. Moreover, actual observations show that a special importance likewise falls to the share of liver extract in anemia complicated by renal disease. In a case of severe secondary contracted kidney with a high degree of anemia and leucopenia, the latter symptom reacted within a few days to administration of liver extract in analogous manner to the leucopenia of pernicious anemia. The leucocyte count rose from 4000 to 10,000, the eosinophils, which were previously altogether wanting, appeared up to 6 per cent. The significant intestinal autointoxication manifest in nephrosclerosis is apparently influenced in like manner by treatment with liver extract, as in pernicious anemia.

The Active Constituent of Glukhorment. — H. H. Dale and H. W. Dudley. (*Brit. Med. J.*, No. 3491 : 1027, 1927.)

Through very careful chemical test and analytical study it was determined that the substance isolated from glukhorment may not be differentiated from the synthalin prepared by Kahlbaum with the methods used. It is either identical with synthalin or so intimately related that laborious chemical analyses with great amounts of material would be requisite for their investigation.

Physiological investigations on rabbits showed that the glukhorment tablets, as they were prepared for therapeutic purposes, either contained synthalin itself or a substance so closely related to synthalin that it could not be differentiated from it by the chemical and physiological methods used. Glukhorment contains this substance in sufficient amount to play an important rôle in any therapeutic or other activity. Concerning the therapeutic value of glukhorment, the authors can give no decision.

Results of Dietetic Treatment of Pernicious Anemia. — R. Seyderhelm. (*Klin. Wochenschr.*, 7 : 1, 1928.)

Organotherapy with liver appears to surpass all therapeutic measures hitherto undertaken for the cure of pernicious anemia. Minot and Murphy are inclined to assume, on the basis of their extensive observations, that liver diet in the treatment of pernicious anemia has the significance of a specific, curative therapy; that it is a question of causal therapy. Minot and Murphy place pernicious anemia parallel to actual avitaminosis in which a causal significance falls to the share of preceding defective nutrition. With regard to the action of liver they come to a like conception as Whipple, according to which an important building material is supplied to the stromata by liver, that is, the supporting substance for the erythrocytes. As actual cause of the pernicious anemia they conceive of a primary disturbance of bone marrow function. With regard to the nature of the active liver substance, Minot and Murphy do not believe that the vitamin E found in the liver by Simmonds, Bekker and McCollum (which is important for the metabolism of iron) is the principle curative of pernicious anemia. Whereas vitamin E is insoluble in water, the liver substance influencing pernicious anemia proved to be soluble in water, precipitable in alcohol, and insoluble in ether. It is free from lecithin, and lipoids, and contains approximately 7 per cent nitrogen, slight traces of albumin and sulphur. The ideal form of liver therapy is, to be sure, the administration of a liver extract which contains the active liver principle. In liver therapy the mechanism of action is still to be determined. It is possible that a substance regulating blood formation, a blood-forming hormone, is present in the liver.

Treatment of Senility and the Dynamogenic Effects Observed in Man by Ingestion of Activated Serum of Young Male Animals. — Ch. Levassort. (*Progrès méd.*, 4 : 160, Jan. 28, 1928.)

The author reports the result of his experiences with M. Busquet's serum in old age. This physiologist has already published the account of the effects of induced masculinization on old roosters and capons by a special serum of young bulls, containing both the circulating hormones of young animals and the antibodies of inhibiting substances discovered by A. Carrel in senile organisms. Ch. Levassort has noted that when administered by mouth 30 minutes before meals, in a dose of 20 cc. per day, the activated bull serum produces in certain depressed individuals and in old people of both sexes, effects of invigoration

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manifested by a greater aptitude for physical and mental work, by a feeling of well being and an optimistic change in disposition.

Insulin Treatment of Diabetic Addison's Disease. — W. Umber. (*Med. Klin.*, **24** : 8, 1928.)

Report concerning clinical experiences in 2 cases of suprarenal disease which were complicated by diabetes without rendering insulin therapy more difficult; moreover, insulin treatment could be carried on without danger of hypoglycemia and with the same dosage as in diabetics with intact suprarenal glands. In the one patient, it was a case of moderately severe diabetes and typical Addison's disease; the second case was that of a diabetic patient with pulmonary tuberculosis and Addison's disease. This case demonstrated in its course that the principle of hyperinsulinization, as it is used for tuberculous diabetics, can also be successfully employed in diabetics with pulmonary tuberculosis and Addison's disease. In all cases, however, it is recommended to introduce the insulin dosage carefully and slowly, in order that an eventually existent insulin sensitiveness such as Unverricht published can be taken into account. The fact that diabetic Addisonians tolerate just as high a dosage of insulin as diabetics with normal adrenals, is not to be explained without further ceremony. It appears as if a compensatory rise of adrenalin production is still possible through hypoglycemia, by which on the one hand the lack of threatening sequelæ of the hypoglycemic symptom complex, on the other hand, also the simultaneous pronounced rise in blood pressure associated with slight hypoglycemia find their explanation.

The Mechanism of Action of Synthalin. — F. Bertram. (*Deut. Arch. klin. Med.*, **158** : 76, 1927.)

Report concerning the author's clinical experience with synthalin in 21 diabetics. In mild to moderately severe cases there resulted an influence on hyperglycemia and glycosuria at the outset. Dyspepsia could be avoided in almost all cases by the use of lecithin-cholic acid. After longer use of the preparation there occurred, however, in the majority of cases a deterioration of the metabolic state. In severe cases of diabetes a favorable influence on the metabolic condition could not be determined in any case. In many cases a marked primary hyperglycemia succeeded even relatively small doses. In three cases precomatose conditions made their appearance with the addition of synthalin and continuance of the therapy employed up to that time (diet and insulin). Following discontinuance of synthalin in the greater number of severe cases of diabetes which were treated with insulin, a similar deterioration of the metabolic condition was noted, so that for the maintenance of the earlier existant equilibrium much higher amounts of insulin than previously were requisite. Severe pains in the vicinity of the liver appeared four times in the course of the treatment. Through experiments on man it can be shown that the blood sugar-lowering action of synthalin takes place through the pouring out of insulin from the pancreas — therefore in the sense of a parasympathetic poisoning. With the administration of sufficiently large amounts of atropin it is possible to weaken the blood sugar-lowering action of synthalin in diabetics, or to entirely destroy it. Instead of this in many cases a marked primary hyperglycemia is observed. Atropin may in individual cases considerably lower the renal threshhold for sugar, so that with examination of the urinary sugar alone, an improvement in carbohydrate tolerance is simulated.

Whereas during the administration of insulin in the diabetic, an extensive sparing of the island apparatus and glycogen deposition are obtained, following synthalin a stimulation of the pancreas ensues and with it exhaustion of the organ which is already damaged. The primary effect of mobilization of blood sugar conditions a decrease of glycogen supplies in the organism. The possibility is discussed that the decrease of glycogen stability, the icterus observed by many authors and the yellow dystrophy of the liver observed by the author merely represent different degrees of a liver poisoning by synthalin. The use of synthalin even in mild and moderate cases is also warned against.

Neuro-Anemic Syndrome. Remarkable Therapeutic Effects Obtained by Whipple's Method. — Crouzon, P. Mathieu and G. Dreyfus. (*Paris méd.*, **17** : VIII, Sept. 10, 1927.)

A new case of neuro-anemic syndrome is reported with spasmodic paraplegia, profound disturbance of sensibility, mental phenomena and cryptogenetic pernicious ane-

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mia. Under the influence of the daily ingestion of 250 grams of boiled calves' liver and exclusive of all other treatment, the asthenia and digestive troubles progressively disappeared; weight increased 7 kilograms, and the number of red blood cells increased from 1,750,000 to 2,800,000 to about 5,000,000. The authors stress the remarkable effects of this new therapeutic method which within 4 months has transformed a bedridden invalid into an individual capable of leading a normal life.

Practical Therapeutics

(*Continued from page 210*)

enzymes, digests albumin bodies, therefore, decomposes dying tissue in a wound not healing by primary intention, that is, it leads to wound cleansing and consequently to healing.

At St. Catherine's Hospital, Surgical Department, in the last 4 months, Roehm's enzyme preparation was used in a great number of cases. Of this number several cases in which a particularly striking effect was obtained with the enzyme preparation are reported:

(1) 62 year-old patient with greasy coated, large ulcers of the leg, which were treated without success with the most varied remedies. The wounds were finally treated with enzyme powder and rest in bed and already with the second change of dressings, the reactive inflammation had disappeared. Then increased secretion of the wound set in; following further powder treatment rapid cleansing, healing over and after 4 weeks the patient was discharged cured. Also in a number of other patients with ulcera cruris favorable experiences were had with the enzyme preparation. Usually powder treatment was used first, and following cessation of the secretion, ointment treatment. Especially good curative result was attained in a decubital necrosis of the scrotum as large as the palm of the hand in a strikingly short time. There is now present only an epidermis defect as large as a cherry; the patient will probably be discharged as cured within a week. Likewise a furuncle was healed very rapidly under enzyme treatment, after it had resisted every form of therapy for weeks. In incised whitlows, furuncles and abscesses, the enzyme ointment promoted wound cleansing to such an extent, that the time of treatment was much shorter than with the use of other therapeutic agents. Greasy, covered and soiled contused wounds are suitable for treatment with enzyme ointment. Frequently such wounds cleanse their wound bed in a very short time and heal up. The action of the enzyme preparation was also very striking in a patient with extensive second degree burns on the face and on both hands. They were treated exclusively with enzyme powder which was dusted on thickly. Also here at first increased secretion appeared, giving place soon to a fresh appearing granulation surface. In a very short time cure resulted, more quickly than would be expected. In any case, it may be said that the experiences which were had with enzyme treatment were good throughout.

Pernicious Anemia of Pregnancy. Treatment by Whipple's Method. — P. N. Deschamps and A. Froyez. (*Bull. et mém. Soc. méd. Hôp. Paris*, **52** : 143, Feb. 9, 1928.)

Pernicious anemia of pregnancy has always been considered one of the most severe forms of anemia. The patient, a woman of 27 years, in the sixth month of pregnancy, entered the hospital on July 22nd, with a typical syndrome of severe anemia and a blood count of not more than 1,800,000. She ingested 250 grams of cooked calf's liver daily from July 25th to August 17th. During this period the blood count rose from 1,800,000 to 5,000,000 and all clinical signs of anemia disappeared. From August 20th to N v. 11th, even though no hematopoietic treatment was instituted, the number of red blood cells did not fa l below 4 000,000.

On October 31st, the patient was delivered at term, under normal conditions, of a living child as well as of a mummified fetus. From a clinical point of view, such an anemia would appear to enter into the class of pernicious anemias of pregnancy. In this case, the onset of the disease occurred insidiously in the first months of pregnancy, the severe symptoms made their appearance towards the sixth month, with appearance of edema, albuminuria, the hematologic picture of plastic anemia, with but slightly marked myeloid reaction and slightly increased leucocytic reaction, accompanied by a tendency to polynucleosis. The authors stress two points in particular: (1) The patient was a primipara, whereas the majority of cases of pernicious anemia of pregnancy occurred in mul-

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tipara. (2) The menses had persisted up to the fifth month.

The evolution of the anemia in this patient differed entirely from the usual course of pernicious anemia of pregnancy. All observations agree in confirming the impossibility of a remission, whatever the treatment instituted may be, so long as the fetus has not been expelled. To the authors' knowledge, there does not exist a case of pernicious anemia of pregnancy in which the blood count rose before delivery. The authors, accordingly, undertook the treatment of such a case by Whipple's method without great hope. Being familiar with the usual absence of any improvement before expulsion of the fetus, they did not dare to employ Whipple's method alone. To it they added the classical treatment of pernicious anemia by transfusion. It appears impossible, however, to attribute the principal effect in the present case to transfusions. The blood cell count increased remarkably (within 29 days the number of red cells increased from 1,800,000 to 5,000,000 in order to continue at 4,000,000 3 months later). It is to be noted that this therapeutic action of calf's liver occurred here in a severe anemia, to be classed among the symptomatic anemias, whereas in the primary opinion of American authors, the method in question would be truly effective only in cryptogenetic pernicious anemia of Biermer's type. This case would seem to represent an argument of great value in favor of the efficacy of liver therapy in the treatment of severe anemias.

Thyroid Insufficiency, Plethora and Polycythemia. — J. García G. Morán. (*Siglo méd.*, **80** : 223, Sept. 3, 1927.)

The patient was a woman aged 58 years. Her menstrual history was normal, although menstruation tended to be profuse. Menopause occurred 18 years ago. Five years ago, following an attack of grippe which necessitated rest in bed for 3 months, the patient noted swelling of the legs, then generalized swelling and tendency to sleepiness. Examination showed intense somnolence. The patient fell asleep everywhere; she was very obese, with spongy appearance and great abdominal plethora; skin, dry and scaly; hands, cold; basal metabolism −27; red blood cell count, 6,120,000 per cubic mm.; weight, 100 kilograms, 300 grams; hypertension; constipation. A diagnosis of thyroid insufficiency was made, with plethora and polycythemia and the following treatment prescribed: two 0.3-gram tablets of thyroidin, daily, with dietary restrictions. Following several months of treatment, the patient showed marked improvement: loss of weight to 83 kilograms; somnolence no longer present; basal metabolism had risen to +5; red blood cell count amount to 3,090,000 per cubic mm.

It is very probable that the case was one of a syndrome of thyroid insufficiency in which the physical appearance and somnolence were the main symptoms. Constipation and profuse menstruation are also symptoms of hypothyroidism. The hypertension appears to be essential; renal function was perfect. Following thyroid treatment to which all other symptoms responded, only hypertension remained unchanged.

The action of thyroid medication on the polycythemia was especially noteworthy in this case. Two months of treatment resulted in a decrease in number of red blood cells from 6,120,000 per cubic mm. to 3,090,000. In this case it is evident that the polycythemia disappeared when the hypothyroidism and plethora had been remedied. Hence, the action of thyroidin in cases of hypothyroidism in which there is polyglobulia is an indirect one and this latter symptom disappears only when the plethora has vanished.

Acid Base Equilibrium in Addison's Disease. — G. Marañon and J. Morros Sardá. (*Siglo méd.*, **80** : 197, Aug. 27, 1927.)

Knowledge of the changes in the blood of Addisonians is increasing daily. Thus, it is well known that these cases are usually accompanied by hypocholesterinemia; that the leucocyte formula changes in the sense of a marked lymphocytosis: the rate of sedimentation of red blood cells is very much accelerated; the blood sugar curve usually reaches low values, etc. It appears, however, that the acid-base equilibrium in these patients has never been studied. The authors examined six Addisonians in this respect and in four of them they found a manifest fall of the alkalin reserve, which consequently revealed a state of acidosis. In the remaining two cases, they encountered values near normal but which also indicated a tendency towards hypoalkalinity. From the study of these cases, they deduced that the fall in alkalin reserve maintains an evident relationship with the intensity of the general disease pic-

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ture, since the reserve was especially low in the patients with most pronounced symptoms and reached almost normal figures in the two patients whose condition was relatively satisfactory.

It is difficult to interpret this acidosis in Addison's disease. It is possible that the tuberculosis infection plays a rôle in these disturbances of the acid-base equilibrium due to the phenomena of proteolysis to which it gives rise. The state of malnutrition in which these patients are found, especially in advanced cases, might also be a factor in the genesis of the acidosis. Another possible explanation would be the retention of poisons of muscular origin which when incorporated into the humors of the body would tend to vary its reaction. Abelous and Langlois and a great number of physiologists and pathologists (Zondek, Pende, etc.) admit that the suprarenals normally destroy or neutralize toxic substances resulting from muscular contraction. As these products are mainly of acid nature, the authors believe that they might be the cause of the acidosis in question. At any rate, the existence of this disorder in Addisonians might serve to explain the poor resistance of these patients to surgical interventions. These facts suggest a trial of alkalin therapy in Addison's disease, especially in advanced forms when acidosis is manifest. Insulin should not be used for this purpose in these cases, because of the extreme sensibility of Addisonians to this medicament, unless great quantities of glucose have been administered previously.

Extension of the Field of Therapeutic Liver Diet. — M. Grossmann. (*Med. Klin.*, 23 : 1851, 1927.)

A patient with most severe cachexia, considerable edema, inability for active movement, severe anemia of hyperchromic type and an amount of urine of 400 to 600 cc. was treated with liver therapy after an unsatisfactory trial of Salyrgan (only transient result and causing headaches), theobromine preparations (without effect) and urea (effective, but causing vomiting). Diuresis rose to 1800 cc. and remained at this level for a long time; it now amounts to 1200-1500 cc. Excretion of sodium chloride rose from 2.5, 2.7 to 5.4 and more per day. To be sure, it showed variations. General condition is good, but there is still no complete recovery, since in the urine cylinders and albumin are present even if there are no more lipoids. The observation speaks in favor of the presence of hormones in the liver. Probably there exists a primary similarity between the effect of the liver on diuresis and thyroidin action.

Johannes von Kries

(*Continued from page 212*)

thought processes of others and his ability to express the splendid ideas he found made his work on "Goethe as a Psychologist" (1924) and on "Immanuel Kant and His Significance for Natural Research of the Present" (1924) worthy of high praise in the realm of criticism. Likewise his interpretation of the work of von Helmholtz ("Helmholtz as Physiologist," in *Die Naturwissenschaften*, 1921) is commemorable. The task of commenting on all the individual writings of von Kries is far too great to be undertaken in this place. The few that are mentioned give an insight into the many phases of his capabilities. Von Kries was not only a prolific writer but a profound one, also. He was a man of few words, and mighty ones; one of his pupils reports that "A short discourse brought us work for weeks to come." He was always a helpful, inspiring leader, anxious to progress to the last limits of a problem, or at least as far as was humanly possible, and to leave it finished thus far so that his followers might take up threads and go on. He proceeded cautiously but surely, not following a battle cry, for he despised showy pretense, but with feet firmly based on the truth and mind alert for all possible contingencies and capable, through its own dominance, of interpreting man, his life and his thoughts.

Concerning Mastopathy of the Male Mammary Glands. — Moszkowicz. (*Münch. med. Wochenschr.*, 74 : 874, 1927.)

Observation of ten personal cases and the review of the literature showed that hormonal incitation is in evidence in diseases of the male mammary glands as well as in the female. Delayed maturing of the testis and premature involution can exert a profound effect on the mammary glands. Moreover, changes in the mammary glands are encountered in simultaneous insufficiency of the internal function of the testis, as well in constitutional (cryptorchidism, hypospadias) as in acquired inferiority (syphilis, tuberculosis, etc.). Finally the author regards the "intersexual individuals" as disposed to mastopathies.

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Eunuchoidism and High Pressure. — W. Seidel. (*Med. Klin.*, **23** : 652, 1927.)

The author describes two cases in which the most important characteristics of the symptomatology of eunuchoidism (Tandler and Gross) were present, namely, overgrowth of the extremities in proportion to body size, scantiness of axillary and pubic hair, with heavy growth of hair on head, genital disturbance and a pelvic formation resembling feminism. The author stresses the fact that the abnormal length of the extremities is not, according to his observations, *a priori* to be taken into account, but only in connection with other eunuchoid symptoms.

Concerning Insulin Shock. — O. Klien. (*Med. Klin.*, **23** : 1776, 1927.)

The course of reaction in insulin shock differs qualitatively and quantitatively in different individuals. Of the objective changes in insulin shock, insulin leucocytosis is especially interesting. It is variously strongly pronounced in different individuals, and always becomes weaker with repeated shock in one and the same individual. In diabetics previously treated with high insulin dosage, insulin leucocytosis also remains absent in very severe shock. In icteric patients, no leucocytosis could be observed in great shock for the most part from the beginning. The insulin leucocytosis is not influenced by the same factors as insulin hypoglycemia. Leucocytosis is set aside only by glucose; insulin hypoglycemia and leucocytosis as well as insulin shock were almost without exception increased by administration of a great amount of water (1.5 liters). Blood sugar fall and rise in leucocytosis followed in steep curves; shock was especially of long duration; likewise the descent of the blood sugar level. Administration of glucose set aside the shock here and the hypoglycemia, but only transiently. It is probably a question of strengthening of the parasympathicotropic action of insulin on the vegetative nervous pathways (effect of fullness of the stomach as vagus stimulus; strengthening of the liver contraction in insulin shock through these latter). In liver disease, the insulin shock is especially powerful and lasting in relation to insulin dosage, likewise the objective hypoglycemia. In liver disease, in insulin shock, the following observations were made: Fall of bilirubin picture often about 3-4 units, shortening of the time of coagulation of the blood, occasionally relative increase in fibrinogen and globulin fraction of the plasma-albumin substance. The thickening of the blood is especially intense in liver disease. Therapeutic use of the influence of insulin on liver activity: Richter observed prolongation of the life of a patient with acute yellow atrophy of the liver under insulin treatment. The author also observed the disappearance or decrease of icterus in the most varied liver affections (cirrhosis, hepatitis, etc.) lasting for months. The relation between insulin shock and change of acid-base equilibrium is not lawful. The alkalosis of the blood, when present, is rather to be regarded as sequel to the shock and not as the cause. In liver disease, for the most part fall of alka'in reserve, despite the most intensive shock with acid-urine reaction. In severe acidotic diabetics rise of alkalin reserve results in hypoglycemia, with shock very slight or altogether lacking. Here, for the most part, one does not succeed in obtaining shock despite hypoglycemia (often with very low blood sugar level) so long as the cholesterin picture of the blood remains high and a lipemia is demonstrable. The urine also remains acid in reaction for just so long a period. After several days of diet rich in carbohydrate, with high insulin dosage, removal of the hypercholesterinemia occurs. With the appearance of hypoglycemia — with normal cholesterin picture — the typical shock takes place, whereupon the actual reaction of the urine changes to alkalin. In two precomatose diabetics, hypoglycemia was systematically brought about daily through overdosage of insulin. As long as the cholesterin picture remained high, no shock occurred despite extreme fall of the blood sugar picture. The reaction of the urine remained permanently acid. First following several days of farinaceous diet with high dosage of insulin did typical shock with normal cholesterin picture set in, upon which the actual reaction of the urine also changed to alkalin (pH equals 7.6). In diabetics previously treated with high dose of insulin, likewise in genuine hydropic kidney disease, the alkalin reserve is for the most part relatively high, the actual reaction of the urine near the neutrality point; hypoglycemia and shock appearing especially mild here (with small dose); especially intensive shock, change in reaction of urine to alkalin appearing according to law! In both cases alkalin enrichment of the organism exists.

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This favors the occurrence of shock; it is, however, not the direct cause and also not the necessary condition for the occurrence of the symptom. The origin of very intensive shock in acidotic liver disease speaks in favor of this, where the alkalin reserve falls in shock with urine reaction remaining acid, as well as in the acidotic patient with renal insufficiency, where with low alkalin reserve (for example, 18 per cent of volume) and strongly acid urine reaction (pH equals 4.5), violent shock was observed. With hypernormal position of the water deposit in the organism, strong diuretic effect is not infrequently noted in insulin shock (for example in edematous kidney disease; in diabetics previously treated with high doses of insulin). A diuresis of 4 to 5 liters and corresponding loss of body weight in 24 hours was more frequently observed. In two edematous renal patients (nephrosis), in whom otherwise diuresis could not be obtained in any way, complete removal of edema followed insulin shock. In addition to water, abundant alkali was also evacuated here. In one case the pH of the urine was 8.0 with an amount of urine of 3 liters.

The Hirschsprung Syndrome as the First Indication of Congenital Myxedema. Several Additional Observations concerning Megacolon Idiopathicum. — J. C. Schippers. (*Monatsschr. Kinderheilk.*, 43 : 289, 1929.)

A 5 year old girl with obstinate obstipation and greatly distended abdomen was underdeveloped physically and mentally. Operative interference was taken into consideration. Striking improvement was derived with thyroid gland therapy, 20 mg. Pulv. gland. thyreoid. sicc. twice daily, and among other things a regular stool passage was obtained. Deutsch is of the opinion that the thyroid gland hormone directly assails the Auerbach plexus and hence the tonus of the wall muscles of the intestine. Biedl observed an increase in intestinal peristalsis after injection of thyroid gland extract. A direct influence of the thyroid gland on the parasympathetic and sympathetic nervous system is indeed quite evident, yet positive proof for this is lacking. Cori points out that the tonus of the vegetative nervous system is raised after injection of thyroid gland extract. Goelin also confirms this.

The Treatment of a Case of Bulbo-Spinal Myasthenia with Extract of the Tuber Cinereum. — M. C. L. Urechia. (*Bull. et mem. Soc. méd. hôp. Paris*, **45** : 784, 1929.)

The author holds it is illogical to administer total extract for the investigation of cerebral organotherapy and thereupon recalls that the total extract of the anterior lobe as well as that of the posterior lobe is to be differentiated. In one case with classical symptoms of bulbo-spinal myasthenia a noteworthy improvement was achieved by means of treatment with an extract of the tuber cinereum.

Discussion on the Severe Hemorrhages following Parturition. — Voron. *Bull. Soc. d'obstét. et gynécol.*, **18** : 357, 1929.)

In hemorrhages following puerperal infection the author unrestrictedly rejects curettage and recommends, instead, the administration of medicinal therapy, for example ergotin or pituitary extract. The medicinal therapy will next be tested in cases where the hemorrhage is caused by retention of the placenta.

Thyrotoxic Myocarditis. — J. Strickland Goodall, and Lambert Rogers. (*Brit. Med. J.*, No. 3468 : 1141, June 25, 1927.)

Most slowly acting poisons which affect the myocardium decrease its tone and usually raise its irritability as well. In thyrotoxicosis the first symptom is usually tachycardia, at first intermittent, then continuous, followed in the later stages by cardiac irregularity, myocardial exhaustion, and even sudden death.

In the later stages of mild cases of thyrotoxicosis, or in the early stages of very acute ones, the heart may become irregular owing to auricular fibrillation and then the normal co-ordinate contraction of the auricular muscle fibers does not occur; the different bands of auricular muscle contract irregularly and more or less independently. The degree to which this dissociation and inco-ordination has occurred determines whether the resulting fibrillation is of the so-called coarse or fine variety. Generally speaking, the condition develops after the disease has been in progress for some years, and must be regarded as indicating that the myocardium is profoundly

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poisoned or that degeneration has definitely commenced. Occasionally Graves' disease starts with auricular fibrillation, and in these cases the condition usually persists. Not infrequently (about 5 per cent) auricular fibrillation develops during or soon after operation on the thyroid, and may occur after any operation, from simple ligation to extirpations of varying extent. Usually the condition is only temporary. Its onset is often synchronous with a rise in blood pressure. On the other hand, cases of Graves's disease which show auricular fibrillation, which may in some cases have persisted for years, are frequently cured of the fibrillation after removal of the greater part of the thyroid, especially if they are treated by quinidine, which appears to influence materially many of these cases after partial thyroidectomy. The cure of fibrillation by removal of the thyroid is a recognized treatment.

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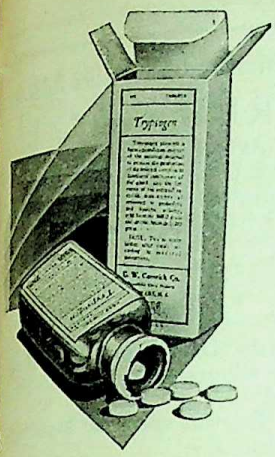
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Pancreas Therapy in Diabetes

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OUR organotherapeutic products are made from fresh glands of healthy food animals, in our own laboratory, under the supervision of competent chemists. All moisture has been removed from these gland products and they will keep indefinitely if contents are not exposed to moisture and bottle is kept tightly corked.

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The Journal of Organotherapy

A Record of Progress in the Study of the Internal Secretions and Metabolism

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Practical Therapeutics

Editorial Comment

Abstracts

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DYSMENORRHEA

THE relief of dysmenorrhea is of primary importance. Long continued pain and the apprehensive dread of each menstrual period ultimately result in a definitely neurotic condition.

"The condition is, therefore, one of continual hammering at the patient's nervous system and eventuates gradually in seriously affecting it. It is no wonder, therefore, that the patients with dysmenorrhea nearly always in time become neurotic." (Prof. William Graves —Harvard Medical School.)

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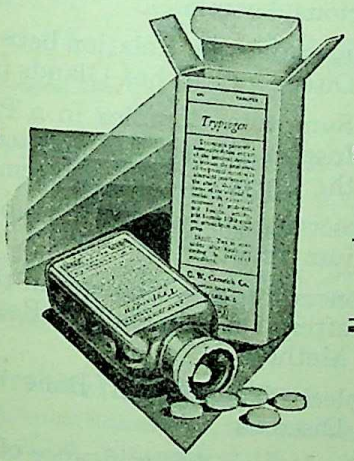
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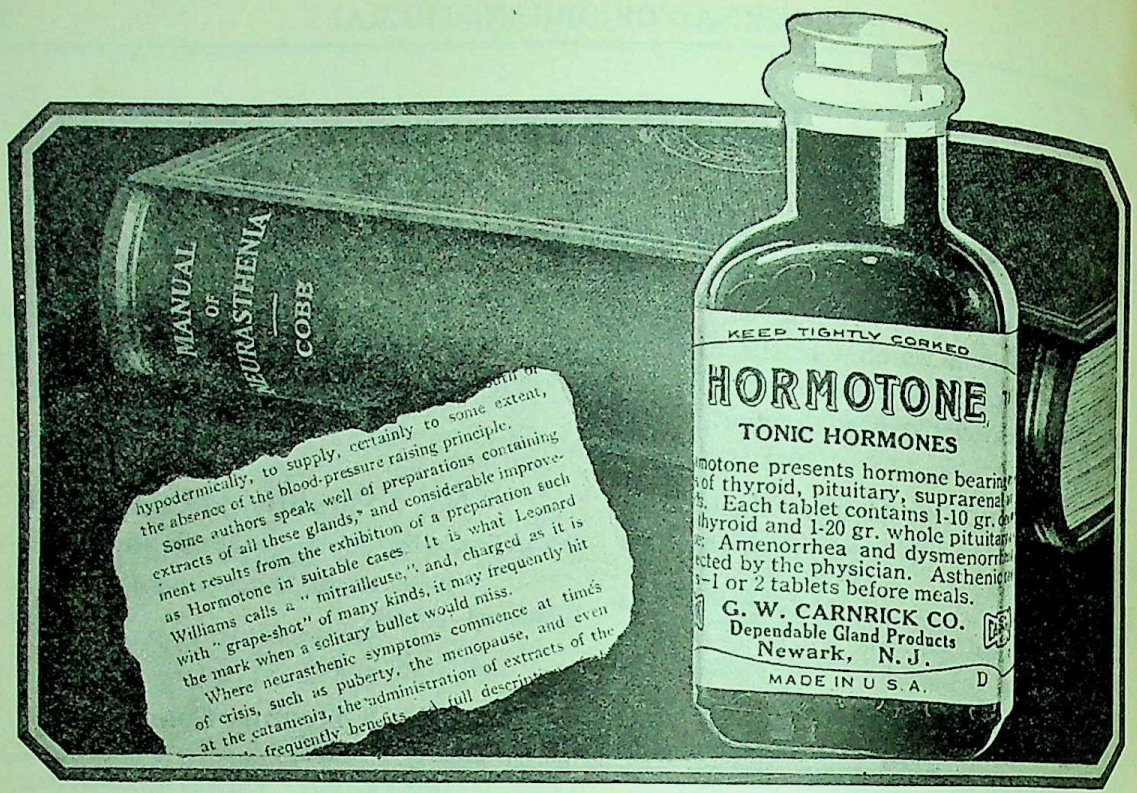
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Menstruation and the Hormones of Ovary and Anterior Pituitary

MENSTRUATION in the human female is attended by certain definite developmental and degenerative changes in the endometrium. These changes depend upon at least two hormones arising in the ovary and two in the anterior lobe of the pituitary. It is not established that estrus in lower animals is equivalent to human menstruation.

DESPITE the indubitable position of importance of the menstruation process in female physiology, it has received remarkably scant attention, compared with other fundamental physiologic mechanisms until very recent times — practically until the last decade. This is somewhat astonishing for menstruation is indissolubly related to and bound up with the process of reproduction in higher animals and thus traces its origin far back in evolutionary history — its biologic necessity arising even with the appearance of the placenta in bisexual reproduction.

Again it is remarkable by reason of the enormous importance of abnormalities of this function in human disease, for there is probably no physiologic mechanism so subject to variations from normal or which demands so much medical attention.

Menstruation appears with and marks the beginning of the period of female puberty

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— the somewhat sudden appearance of fully developed sexual maturity. Indeed menstruation together with the changes in the ovary may be regarded as the important physiologic phenomenon of puberty. The ovary, as is well known, has a direct causal relation to menstruation: ablation resulting in absolute cessation of menstruation which may again be induced by transplantation of an ovary. This fundamental observation also established another vital point. The ovary exercises its control over the menstrual process by means of some substances elaborated into the blood and not by any nervous mechanism. Widespread research on the internal secretion or secretions of the ovary responsible for the changes of menstruation have resulted in some positive additions to our knowledge. The ovary elaborates at least two hormones, one the follicular or "Allen-Doisy" hormone and one the luteal hormone. Both, as will be seen, exercise fundamental and different effects on the process of menstruation. Within recent years another endocrine tissue — the anterior lobe of the pituitary — has been related to the process and there now remains no doubt that an anterior pituitary hormone is a normal and necessary factor in the endocrine mechanism controlling menstruation. This pituitary action seems almost certainly to be exerted through the intermediary of the ovary.

Another internal secretory effect and one of which less is known, is that produced by the ovum itself or the trophoblast formed by its implantation on the uterine mucosa.

These various factors have been interrelated in different schemes of action by several of the contributors to the field. It is not yet possible to formulate precisely the manner of interaction of these several factors, but there has been accumulated a substantial mass of facts relating to each of them individually. We can not assign a "cause" for menstruation from a closed cycle of interrelated factors. About all we can hope to do is accurately to establish the sequence among them and describe the details of the process. In the description of ultimate facts in any science, however, this is what we do. We can frequently describe the "how" but not the "why."

The structural changes taking place in the uterine cycle are described by Marshall (1) as follows:

"(1) The constructive stage.
"(2) The destructive stage.
"(3) The stage of repair.
"(4) The stage of quiescence.

"During the constructive stage the uterus undergoes growth, glandular development, and hyperaemia, *i. e.*, increase in the blood vessels, both in size and in number. The changes in a general way are described as being very similar to those which occur at the commencement of pregnancy.

"At the beginning of the destructive stage the congested vessels in the uterine mucosa break down, and blood is freely extravasated in the tissue. It subsequently forms large lacuna-like spaces in the superficial part of the tissue, and then the epithelium ruptures and bleeding takes place in the cavity. The whole, or a great part of the superficial epithelium, is removed as a result of the extensive haemorrhage, and a varying amount of underlying stroma tissue may also be torn away, leaving the lumen of the uterus bounded by a raw edge. The discharged blood, together with degenerate epithelial and stroma cells, constitute the menstrual clot, and this along with a sanguine-mucous flow passes down the uterus and through the vagina to the exterior. The amount of blood lost in a woman is on an average about three ounces, and the discharge lasts from three to six days. The uterine glands are active during menstruation and contribute to the discharge. When the tissue denudation is exceptionally great the condition is known as *menorrhagia*, and when it results in a painful condition it is called *dysmenorrhoea*.

"During the next period, repair sets in, the epithelium being renewed either from cells which did not suffer destruction in the pre-

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ceding period or from the cells of the glands. At this stage the blood vessels become reduced in size and number. The stage of repair is followed by a stage of apparent quiescence, but it seems probable that in many individuals the uterus commences to undergo growth changes which are continued in the succeeding constructive stage."

Now, what are the relations of the ovary and anterior pituitary to these cyclic changes in the uterus?

The purpose of the whole process is, of course, reproduction and we may begin with ovulation or the discharge of a matured ovum from the ovary. This event has been held to be essential to all of the succeeding changes in menstruation. Recently, however, evidence has been presented that tends to vitiate the importance of the ovum in the process (2), although, as will be shown later, the validity of this evidence is questionable.

"In spite of a great deal of circumstantial evidence of this sort, however, this theory of the essential rôle of the ovum in menstrual periodicity must give way, it seems to me, before certain facts which have apparently been established. One of these has already been referred to: the occurrence, at least in monkeys, of definite periodic bleeding with no sign of ovulation, and, for that matter, after apparent destruction of the entire follicle apparatus by roentgenization of the ovaries. In the case of some animals at least, there is some evidence, which, however, needs substantiation, that the sex cycle can continue after complete castration (Halban, *Zentr. Gynäkol.*, 35 : 1585, 1911). There have also been reports from time to time, especially in the older gynecologic literature, of the persistence of human menstruation after removal of both ovaries. Most of these, however, have been unconvincing, because of the ever-present possibility that ovarian tissue had been left behind, or that supernumerary ovarian tissue was present.

"A number of observers have reported that the tubes of an animal are ligated or excised so that the ovum cannot enter the generative canal after its discharge from the ovary, the sex cycle continues normally. This experiment is a rather obvious one from the human standpoint, for the same conditions and the same results are seen in the innumerable cases of salpingitis with completely sealed tubes, often necessitating excision. Such experiments do not, of course, eliminate the possibility of the continuance of a hormonic influence from the ovum even if it is lost in the peritoneal cavity. This factor can, however, be eliminated by allowing the ovum to enter the tube and then washing it out. The experiment has been done by a number of investigators, and even in the human subject evidence along this line is available in the work of Allen and his associates (Allen, Pratt, Newell and Bland, *J. Am. Med. Assn.*, 91 : 1018, Oct. 6, 1928), who first successfully removed human ova from the tube. In their cases, even though the ova were thus washed out, the sex cycle was undisturbed.

"Again, the recent studies of the results of anterior pituitary implantations on the ovary and the generative tract indicate that, even in immature animals, the phenomenon of estrus can be elicited by the simple impetus of the implantation, while the ova appear to play a rather passive rôle. These experiments would seem to establish that the ovum is not the underlying factor in menstruation, though they do not in themselves eliminate it as a factor in its periodicity.

"Finally, in the only report as yet available on the subject, that of Allen, Pratt and their co-workers, there would seem to be serious doubt whether the human ovum lives more than a short time after its discharge from the follicle. In all cases in which the ova were washed out from the tube, the operation was done at about the middle of the cycle, *i. e.*, only a few days after ovulation, and other evidence supported this belief. Yet all the ova already showed signs of definite degeneration. Certainly it would seem difficult to believe that the ovum can retain its vitality for

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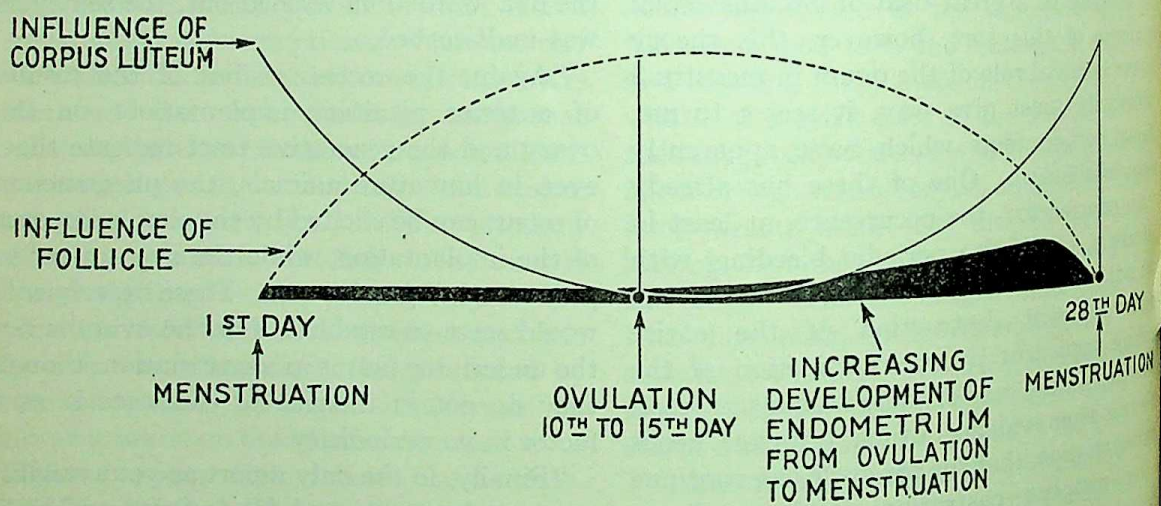
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the two week span formerly accepted. These observations are as yet too few in number to constitute an imposing array, but they must, with the other evidence I have mentioned, impel us to search for some other underlying factor than the ovum." (Novak (2).)

Ovulation takes place about the middle of the menstrual cycle, *i. e.* on the 13th or 14th day of the 28 day cycle. At the time the uterine mucosa undergoes hypertrophic changes suitable for the reception of the ovum. These changes have been gradual and began immediately after the last preceding menstruation. They correspond to the changes described under (1) constructive stage above. Immediately after the extrusion of the ovum the graafian follicle undergoes definite organization with the formation of a new type of tissue, the corpus luteum, and this gives rise to an internal secretion which plays an important and necessary part in the subsequent changes.

The influence of the internal secretion of the corpus luteum begins, therefore, in the intermenstrual period and increases up to the next menstrual period when it degenerates.

Another active internal secretion of the ovary, the follicular or "Allen-Doisy" hormone, also plays an essential, although entirely different, part in the process. This hormone is found (largely at least) in the follicle during development of the ovum and therefore exerts its action at a different period of the cycle. The time relationship of these several factors together with the development of the uterine mucosa is shown graphically in the diagram reproduced from this Journal (Vol. XII, No. 1).



We may inquire as to the nature of positive evidence of the presence of these several postulated hormones, the follicular and the luteal, from the ovary, two from the anterior pituitary and possibly one from the ovum itself.

Of the follicular hormone (folliculin, estrin or "Allen-Doisy" hormone) there can be no possible question. Prepared first by Allen and Doisy, and by Zondek and Laquer and later by a host of workers all over the world, its existence is indisputable. Precise biological assay is possible and its effects are unmistakable. Frank and Goldberger have demonstrated the presence of this hormone in the blood of women and have shown that there is a cyclic accumulation in the blood reaching a maximum just before menstruation.

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In amenorrheic women this accumulation of hormone to a "threshold" point is definitely absent. The follicular hormone is estrus-stimulating. Moreover, in the light of recent research it seems to exert a necessary action on the endometrium, supplementary to the hormone of the corpus luteum in inducing the changes of progestational proliferation. This is important if it is true as proposed by Johnstone that estrus changes and reproductive changes are two different processes. While such an effect supplementing the action of the luteal hormone in the endometrium makes the follicular hormone a factor in menstruation of the human type and in which the influence of the corpus luteum is indispensable it should be noted that it is primarily a hormone inducing estrus, which may be an entirely different phenomenon from menstruation. Thus its chief effects (at least in lower animals) are related to changes in vaginal epithelium rather than the uterus — the method of its assay by Papanicolaou and Stockard depending on this fact. The uterus, however, shows some hypertrophic changes, which require the additional effect of the luteal hormone to bring about the decidua characteristic of true menstruation.

Concerning the hormone of the corpus luteum there would seem to be no less certainty than of that of the follicle. Much of the earlier work suggestive of a definite luteal hormone was based upon the constant relation of the development and degeneration of the corpus luteum to the uterine changes resulting in menstruation.

In animals extrusion of the corpus luteum by squeezing hastens the estrous period. Persistent corpora lutea suppress ovulation and their expression results in reappearance of estrus. In the human female persistent corpus luteum inhibits menstruation. Much evidence of this kind is available. Further proof of a luteal hormone has been presented in the preparation of active luteal substances exerting definite estrus-inhibiting effects. Papanicolaou (3), Parkes and Bellerby (4) and Allen (5) have been entirely successful in preparing such extracts. The action of the luteal hormone is described by Papanicolaou as follows:

"The proper luteal hormone and the female sex hormone act in an entirely different way from each other and are, to a certain extent, antagonistic. The luteal hormone inhibits and delays ovulation and estrus, whereas the female sex hormone rather accelerates these processes to a limited extent. The luteal, in a purified state, does not excite estrus and does not cause hypertrophy in the genital tract of spayed females, as the female sex hormone does to a striking degree. Both are active during pregnancy, but act in different manners. The one inhibits, the other stimulates. The two, however, act simultaneously. The oral administration of extracts containing luteal hormone gave no results, though large doses have been used. From a practical point of view, this method of administration cannot be utilized at present."

More recent work on the subject, however, casts some doubt on the antagonistic relationship between the two hormones. Rather, it would appear that the corpus luteum supplements and continues at a later period the effect of the follicular hormone of an earlier period. This point of view is presented by Hisaw and Leonard (6).

"From the data presented in this paper it seems quite clear that the progestational proliferation characteristic of the rabbit uterus during pseudo-pregnancy is the result of a combined effect of follicular and corpus luteum hormones. The function of the follicular hormone seems to be that of putting the uterus into proper physiological condition so it can respond to the corpus luteum hormone. Neither of these substances can produce progestational proliferation in the castrate uterus when given alone. If, however, the castrate uterus is first brought into the condition typical of oestrum through the injection of follicular hormone and is followed immediately by corpus luteum treatment, progestational

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proliferation results. It also seems that a quantitative relationship between the follicular and corpus luteum hormones must exist for the prolongation of the progestational picture over an extended period."

Allen (7) and Allen, Pratt, Newell and Bland (8) give a similar conclusion. Weichert (9) found that progestational proliferation can be induced by the luteal hormone if the follicular hormone has previously been injected, but only a negligible number respond to the corpus luteum alone. He sensitized the uterus of the unmated rat in the diestrous cycle by corpus luteum extracts as well as ovariectomized animals in which estrus had been induced previously by injection of the follicular hormone.

The influence of the hormone of the anterior pituitary has been demonstrated more recently. Although some correlation of function between the pituitary and ovary had been suspected as a result of clinical observation and physiological changes, the actual demonstration of an active hormone, extracted from the anterior pituitary and exercising definite effects in the ovary, was first made by Evans (10). His experiments showed that the anterior pituitary hormone in addition to growth-promoting effects suppressed estrus and induced luteinization of the graafian follicles without preceding ovulation. The ovaries therefore showed larger number of organized and luteinized corpora lutea with vestiges of ova still remaining.

Teel (11) extended these observations and gave evidence of the effects of anterior pituitary hormone in producing corpora lutea which were functional in producing placentoma as first described by Leo Loeb.

"1. Under the conditions described, the daily injection of anterior hypophysial fluid always brings about a typical decidual cell response to injury of the uterine mucous membrane in animals in which the ovaries are present.

"This response does not occur when the ovaries are absent."

Smith (12) by transplantation methods further demonstrated the pituitary-ovary relationship.

"Daily homoplastic transplants of the pituitary from the adult, given intramuscularly, induce sexual maturity in the female rat as early as the weaning date (22 days of age), thus transcending all normal variability. Animals which are but fourteen days of age when treatment is begun mature sexually in from eight to ten days; when treatment is begun at the weaning date they mature in five to six days.

"The opposite response of the sex apparatus results from pituitary ablation before sexual maturity, the complete establishment of the vaginal canal being delayed and the genital system remaining undeveloped.

"2. The anterior pituitary component of the transplant only, is essential for the induction of premature sexual maturity, the posterior lobe of the pituitary neither hindering nor aiding in the response.

"3. No stimulus to the development of the uterus or vagina of the immature ovariectomized rat is given by these transplants.

"4. The invariable and rapid maturity which is induced by daily pituitary transplants speaks against the view of those who maintain that hypophysectomy does not interfere with sexual development or function, and indicates an important hypophyseal-gonadal interrelationship."

Zondek (13) finds that the anterior pituitary produces a growth hormone, concerned with the somatic growth (also reported by Evans and Simpson) and two sex hormones (or at least there are two factors bound up in the sex hormone). He calls them A and B. The first is concerned in maturation of the follicle and the second in causing luteinization. The A factor is not characteristic of pregnancy and may occur in the urine in non-pregnant women. The B factor has been constantly demonstrated in the urine of pregnancy and Zondek and Aschheim have developed a test for pregnancy on this basis.

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Hormone from the urine of a pregnant patient is injected into immature female mice and gives characteristic changes in the ovaries.

Zondek and Aschheim (14) also made implantations of the anterior pituitary of mice and succeeded in inducing early estrus. They concluded that the effect was exerted only through the ovary which undergoes early maturation and elaborates follicular, estrus-inducing hormone. Now, whereas Zondek and Aschheim, and Smith clearly showed induction of precocious sexual maturity, the ripening of the large number of graafian follicles and ovulation, Evans, as noted above, found suppression of ovulation and luteinization of the follicles leaving the ovum imbedded in the follicular mass. This discrepancy is doubtless due to the different methods of supplying the hormone of the anterior pituitary — implantation and injection. Evans and Simpson (15) describe this as follows:

"Precocious maturity had been secured by the implantation of perfectly fresh warm rat glands; growth by the administration of various extracts of 8 hour old bovine glands. The markedly different results from these two procedures could have been due to the freshness or staleness of the glands used, the source of the glandular material (rat or bovine), or the method of preparation of the material. We can show that the latter explanation is the correct one. Both hormones reside in the anterior hypophyseal tissue from either source, rat or bovine, and specific extractives can be used for either. The growth hormone cannot easily escape from the relatively large tissue fragments used in the implantation method, but it can readily do so when this tissue is merely triturated, and extraction of rat glands in a way identical with that employed in the bovine growth extracts showed a similar abundance of the growth hormone in the tiny glandules. If the implantation method is employed (*i. e.*, whole rat or similar sized portions of bovine glands introduced intramuscularly), double the weight of substance essential for satisfactory growth extract will not confer growth. On the other hand, implanted bovine glands stimulate precocious sexuality as do rat glands and but little diminution in this hormone occurs with six hours "aging" after the death of the donor. It has furthermore been possible for us to secure the maturity-provoking or sex-stimulating anterior hypophyseal hormone by extracting this tissue in ways different from that employed for the growth hormone, and successful extracts of the second hormone had been employed by us before the very recent publications of Zondek and Aschheim (*Klin. Wochenschr.*, 7 : 831, Apr. 29, 1928) indicating partial purification of this substance."

Without question these and other experiments prove that the anterior pituitary acts through the ovary and not directly on the uterus. Moreover, the factor initiating the ovarian changes is not resident in the ovary itself but in the anterior pituitary.

The Ovum and Menstruation. — It has been shown that the anterior pituitary exerts a primary influence in causing ovulation and the subsequent ovarian changes, and without doubt in normal human menstruation this constitutes the regular scheme. Nevertheless, in the menstruation of monkeys Corner (16) and Hartman (17) have shown that monkeys with apparently normal menstruation presented no signs of a preceding ovulation, of a graafian follicle or of a corpus luteum. Against this is the criticism of Robert Meyer that this type of bleeding in monkeys is not analogous to menstruation in women. Corner describes this type of bleeding (menstruation?) as not associated with the characteristic progestational changes of the endometrium resulting from a corpus luteum.

"In young mature females of the monkey, *Pithecus* (*Macacus*) *rhesus*, menstruation frequently occurs without ovulation, and is therefore not dependent on the presence of a corpus luteum. However, when ovulation occurs, it seems to take place at a definite time, about twelve or fourteen days before the onset of menstruation. Menstruation without

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ovulation is not preceded by the so-called premenstrual changes of the endometrium, which occur only after formation of the corpus luteum. The cause and meaning of menstruation, in this species, are not at present known."

R. W. Johnstone (18), as well as Meyer, holds that the cyclic bleeding of monkeys is not analogous to human menstruation. His views as to the independence of estrus and its changes from the reproductive function of which menstruation is a part are as follows:

"In approaching the subject, the first point which requires to be clearly apprehended is that in all female animals the generative organs, taken as a whole, have two distinct functions to subserve. One is the sexual or copulative function, whereby the female receives the male gametes into her genital tract; and the other is the reproductive function, which begins with ovulation and includes gestation, parturition, and lactation. We must keep these two functions quite distinct in our minds, for upon that distinction depends our understanding of the problem. In the lower mammals both the sexual and the reproductive functions occur at regularly recurring intervals, so that we have what we may call a sexual cycle and a reproductive cycle, each essentially distinct from the other.

"The sex cycle of the lower mammals is characterized by the regular recurrence of periods of estrus or sexual desire, and for the performance of the sexual act the genitalia of the female require special preparation. The opening of the vagina becomes enlarged, the vaginal epithelium becomes cornified, the uterus becomes enlarged and congested, and the secretions of the genital tract become increased — all with a view to the reception of the male gametes and to facilitate their swimming up into the oviducts. After the sexual congress, which almost inevitably occurs at this period in animals living in a state of nature, the genitalia begin to regress, and in some species there is actually a sanguineous discharge at this regressive stage, due to the congestion of the whole genital tract. It was the regular recurrence of this discharge, along with the other phenomena, which has led to its being generally regarded as the analogue of menstruation in the primates and in the human female; and while the analogy is tempting, I believe it to be incorrect.

"The second or reproductive function begins with the maturation and dehiscence of the ovum, and in all mammals ovulation is followed by a series of changes in the ovary and the uterus, designed to prepare for the nidation and gestation of the fertilized egg or eggs, changes consisting in the development of the corpus luteum in the ovary and in the vascularization and sensitization of the endometrium of the uterus and its metamorphosis into what we call the decidua. If the fertilized egg is forthcoming, and in the lower animals living in a state of nature it may be assumed that it almost always is, the reproductive cycle continues over the period of gestation and lactation and ends by the return of the ovary and uterus to their 'resting' condition, in readiness for the repetition of another reproductive cycle."

Johnstone believes therefore that bleeding alone does not constitute menstruation and that the ovum is a necessary link in the endocrine chain causing menstruation:

"I submit that the link must be some hormone formed by the trophoblast of the young ovum and that this in all probability, stimulates the corpus luteum not only directly but through the medium of the anterior lobe of the pituitary body."

The entire process of menstruation and its several factors may now be briefly considered. Since the ultimate aim of the whole process is obviously reproduction it does not seem difficult to regard the cyclic menstrual flow and preparation of the endometrium as a result of failure of impregnation and it is now common to regard it as a pseudo-pregnancy. Every element proceeds just as if a

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real pregnancy were to occur and in the absence of impregnation the preparatory stages are discarded and preparations made for the reception of a new ovum. The process then is essentially a pseudo-pregnancy. The relationship of this process to estrus of the lower animals is made clear. According to Johnstone (quoted above) menstruation is not at all analogous to the bleeding of this pre-estrus, and "is essentially free from any causal connection with any trace of an estrus cycle."

The pseudo-pregnancy theory, of course, presupposes ovulation and the subsequent influence of the corpus luteum and since Corner's observation of menstruation (?) without ovulation (and corpus luteum influence) does not seem definitely to identify the bleeding of monkeys with menstruation in the human female (see his description of the process above), it would seem that the pseudo-pregnancy theory is still tenable. The changes of estrus are characterized by changes in the external genitalia and vaginal epithelium which bleed when the period of engorgement has passed. It does not appear that this type of bleeding is sufficient to identify it as menstruation which in the human female is characterized by a very definite development of the endometrium from which the bleeding later occurs.

Since the anterior pituitary is the "motor of the ovary" we may start with it in following the process. Two hormones are formed there: one exerts an action on maturation of the follicle and one on luteinization and growth.

The first pituitary hormone stimulates maturation of the follicle and ovulation and there is a large production of the follicular hormone. The follicular hormone accumulates in the body and exercises a sensitizing influence on the endometrium, and a cornification of the cells of the vagina. The second pituitary hormone acts on the graafian follicle following ovulation and luteinizes that structure, which then elaborates the luteal hormone. The luteal hormone represses further ovulation or maturation during the latter half of the 28 day cycle and further acts on the endometrium (first sensitized by the follicular hormone) exerting an effect of development and preparation for the ovum. The luteal effect and the hypertrophic, endometrial, progestational development proceed together and just before menstruation the corpus luteum degenerates and the hypertrophic endometrium likewise undergoes retrograde changes, bleeding, and sloughing off and a new cycle begins. During the whole period there is apparently an increasing concentration of follicular hormone which reaches the maximum just before menstruation. It acts as a supplement to the luteal hormone in preparing the progestational changes of the endometrium, induces estrus changes in the vagina, and apparently finally, at its point of greatest concentration has some part in inducing the degenerative changes preparatory to the menstrual flow (perhaps both on corpus luteum and on the endometrium. If this is true it is in effect antagonistic to the corpus luteum but is able to destroy it only when present in maximum concentration. Its action on the endometrium earlier, however, is necessary to supplement that of the corpus luteum.)

The interaction of the several hormones of the anterior pituitary, ovary and perhaps of the trophoblast of the imbedded ovum become practically certain. The mechanism begins to be vaguely understood, but much work remains before it can be precisely formulated.

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(*Concluded on page 306*)

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Clinical Observations concerning Respiratory Basal Metabolism

(Translated from the article by Prof. F. de Quervain and Dr. F. Pedotti, First Assistant Physician at the Surgical Clinic, Berne.)

(*Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 39 : 646, 1926.)

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(Continued from Vol. XIV, No. 4)

If cretins generally show a metabolism slightly lower than cases of acquired myxedema, it must be recalled that, as mentioned, the metabolism values obtained from these are rather too high. On the other hand, it is clear that with them conditions obtain which are different from those in acquired myxedema. In the case of cretins we have before us, from childhood, a partial progressively defective thyroid gland with which the organism has plenty of time to accustom itself and certain compensation can be reckoned theoretically. However, despite the elimination of the more severe cases in which metabolism could not be tested, the fact that the average value lies so far under the normal at once shows us (in agreement with the histological findings) the importance of the thyroid gland insufficiency for the disease picture of cretinism. We stress this therefore, since from various sides, most recently from Finkbeiner, the pathogenetic importance of the thyroid gland defect for cretinism is always more or less doubted, even, is not accepted.

Up to the present the experiments undertaken on cretins have been concerned chiefly with albumin and mineral metabolism, while the investigations on the gas metabolism of endemic cretins is still totally lacking. In accordance with the case of cretinism investigated by Magnus-Levy it may be said that the individual had practically no thyroid gland, so that it was really a case of sporadic athyrosis. The work from the Koch Clinic is likewise concerned with albumin metabolism. In his enlightening experiments on the metabolism of albumin and minerals Scholz comes to the conclusion that perhaps cretinism lies "behind the myxedema" and that the oldest cretin behaves indifferently toward myxedema. With a view to the gas metabolism, one can say, in the main, that many cretins have never passed through the myxedema in the strict sense of the term, but by their own efforts they have corrected their metabolism for the disposal of the existing thyroid function.

In two cretin cases the *iodin* action and the *thyrakrin* action were checked. The results were as follows:

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O. M., 30 yrs. old, goiter cretin, not operated. Basal metabolism.	H. F., Male, 13 yrs. old, half cretin, Str. nodosa parenchymatosa. Basal metabolism.	W. M., 14 yrs. old, female cretin, not operated. Basal metabolism.
31/5/22 ..... −16% 4/6/22 ..... −31% 22/6/22 beginning of iodin cure, 0.05 potassium iodid per day. 28/6/22 ..... −0.68% 7/7/22 ..... −3.4% 8/9/22 ..... −2.2% Thus a strong influence of the intense minus value.	31/10/22 ..... −0.7% From hence 0.1 potassium iodid per day 7/11/22 ..... −2.2% 14/11/22 ..... −3.7% Thus no influence on the gas metabolism. The slight fall arises from improvement in the use of the apparatus.	16/6/22 −22.4% From 21/6/22 on 1 tablet of 0.3 Thyrakrin Oswald per day. 29/6/22 −10.9% 6/7/22 −0.7% Thus strong influence of the minus quantity.

We do not wish to draw any extensive conclusion from these isolated investigations. After all the presentation of these facts confirms the results, in accordance with the opinion of de Ligneris and partly agrees with the report of Breitner, that iodin mobilizes the thyroid secretion. The negative result in the second experiment may arise from the colloid impoverization of the gland and from the brevity of the experiment, especially considering the small dosage in so short an interval. The test should be tried again.

That thyroid gland preparations increase the gas metabolism is a fact well tested by an abundance of exact, quantitative experiments on thyroxin, performed in the laboratory of the Mayo Clinic. The example cited here illustrates the importance of the B. M. determination. The influence of thyrakrin was not such as to detract from the pulse frequency or the volume per minute, for apparently neither was influenced. The volume per minute even decreased after familiarization with the apparatus!

5. Cretinism without Goiter

In cretins without goiter we find exclusively minus values, yet even in these instances, four times, we find values between null and −10 per cent, thus lying in the valid region. Here, too, mention must be made that the values are too high, for the cretins lacked comprehension for the experiment and that most of the worst cases could not be investigated.

In cretins without goiter the thyroid gland is atrophic, histologically, but even at that, as the tests on tadpoles (Branovacky and Branovacky-Pelech) have shown us, it is not inactive. It is not sufficient because of the small volume, but it does perform a little, so that it is not necessary for these patients to experience the myxedematous stage. Nevertheless, this stage is often rather pronounced and lasts a long time. We have then to deal with various quantitative degrees and qualitative forms of insufficiency in which, perhaps, extra-thyroidal compensation processes also can be instituted. As the stereotype picture of the athyroidal individual indicates, these are quite inadequate. The total disturbance is on the average more severe than in goiter-bearing cretins, who often possess, besides the remaining atrophic gland, a certain amount of partially functioning goiter tissue for the process.

In the case of dwarf cretins the question may ultimately be raised whether the standard values can be employed off-hand in these cases. From the systematic investigation of dwarfs in whom the disturbance of growth has nothing to do with the function of the internally secreting glands, this can be determined. Such experiments have not yet appeared, however, and are not easily obtained in sufficient number for the cases are rare. The two cases of dwarfism investigated by Stähelin and Gigon are not free from objection as regards the thyroid gland, and therefore can not be applied comparatively.

We shall take up this point again elsewhere and we shall discuss in a special section the rôle of the body length in the determination of gas metabolism results, as applied to our particular material.

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6. Operated Basedow Cases and Common Goiter

This group contains some seven cases of Basedow, operated from 1-13 years previously, of various geographical distribution, whose average basal metabolism was −5.1 per cent, with limiting values of +4.7 and −9.1 per cent. The other average values are: Pulse 70, volume per minute 5.2, respiratory quotient 7.7, quite normal values. Two cases of common goiter, operated several years previous, with slight symptoms, indicated a basal metabolic value of −14 per cent and −15 per cent. In these nine cases the gas metabolism determination was not made before operation.

To this group may be added several comments concerning the *consequent experiments on Basedow goiter and various other struma previously tested by us.*

In Basedow goiter, the basal metabolism in nineteen controlled cases after tissue reduction operations, runs from an average of +36.6 per cent down to +7.9 per cent, thus signifying an average reduction of 28.7 per cent. Total ligature and then rest in bed for 14 days resulted in a significant, though slight decrease. A drop from +71 to +21 per cent was observed after 14 days rest in bed and the administration of 2-5 mg. iodin per day. We waive any claims here to the average results obtained because the experiments are so few and because a great amount of material has been observed, particularly in the American clinics (Mayo, Crile, etc.). Our material merely confirms what is already known.

In the matter of common goiter, only six cases were checked after operation and there was found, on the average of 30 days a drop of about 7.8 per cent.

In cretin goiters two checks were done which gave decreases of 1.1 per cent and 11.2 per cent. In both these cases we had to abandon the follow-up experiment for the reason that we had to dismiss the patients on other grounds — lack of room — usually a week after the operation, *i. e.* too soon to render them suitable controls.

7. Diverse Cases

Under the thirty-four diverse cases we have differentiated three sub-groups which have a particular interest, namely they are cases with *hypogenitalism, genuine adiposity* and *neurasthenia.* The remaining cases are divided according to various pathological conditions.

(*a*) *Male Hypogenitalism*

This group contains seven cases of underdevelopment of the external genital organs, from 11-55 years of age, belonging to the adiposogenital type, with vast fat deposits. Hypophysials in some normal, in some small. The average values are: Pulse 76, volume per minute 5.8, R. Q. 0.80, B. M. −10.95. These findings agree with those of Means, Marañón and Carrasco, Tierney and others, while Plant, Liebesny and Schwarz, Zondek and Löwy find partly normal values in their fat experiments in hypophysials. In these cases it is difficult to keep the direct influence of the hypophysial glands separate from that of the atrophic sex gland. The experimental researches of Asher and Bertschi on rabbits found no impression of the sex glands on the respiratory metabolism. According to Korentschewsky, one must assume an indirect association concerning the thyroid gland, while the removal of the sex glands remains ineffective, with coincident removal of the thyroid, with the presence of the latter, in contrast, the respiratory metabolism is lowered.

(*b*) *Female Adiposity*

This group embraces seven cases including two border cases. Four female patients from 11-22 years of age, all southern European origin, present a concordant aspect: Tendency to lay on fat, easily fatigued, mental apathy, and also signs of nervousness. Average intelligence, non-myxedematous type. The average values are: Pulse 72, volume per minute 5.4, R. Q. 0.79, B. M. −20.5. The basis for this condition may well lie in the

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thyroid gland, though we have no anatomical foundation for this assumption. Thyroid gland preparations seem to have a favorable action. Marañón assumes in such cases as these, a pluriglandular disturbance in which the ovary and thyroid glands play a leading rôle, and designates it as "juvenile ovary insufficiency." These cases deserve to be observed for a long time for their respiratory metabolism.

Included with these there are: One case of obesity in a 25 year old woman, from the south, with a B. M. −8.4 per cent, who can hold place in the above group, a case of common obesity with B. M. +8.7 per cent and a female case of adiposogenital type with B. M. -10.7 per cent. (In this case also, perhaps, there is thyroid gland insufficiency: Struma cystica, little healthy thyroid gland tissue.)

(c) *Neurasthenia*

This group contains five cases with basal metabolic values within normal limits (−3.9), indeed, with a pronounced tendency towards the minus side. In this instance, however, the volume per minute and the respiratory quotient show nothing particular.

(d) *Remaining Cases*

The following may be emphasized as interesting concerning the remaining cases called "varied."

One case each of *Little's disease* and *Parkinson's disease*, both with +14.7 per cent, which is not to be wondered at considering the muscular activity.

One case of *iodin idiosyncrasy*, one of *Morbus Darier*, one of *dermatitis herpetiformis* with normal values (−0.5 — +6.4 per cent).

One case of *scleroderma* with histologically normal thyroid gland: −11.0 per cent.

Two cases of *infantilism* which had been treated with thyroid gland preparations, with +4.3 and +4.7 per cent.

One case of *climacteric complaints* and puffiness, without evident myxedema, with +4.3 per cent (tested during treatment with thyroid gland).

A *constricting struma in a case of 8-months pregnancy*, with stridor: +30.9 per cent, in which case tracheostenosis and pregnancy were participating to increase the basal metabolism value.

A *proliferating struma according to Langhans* with +41 per cent, which dropped to −11 per cent after operation.

Finally, one case in this group deserves particular mention for it does not entirely fit into any other.

Female patient of 36 years, qualified as tachycardia, struma, slight exophthalmos, treated for 2 years as a Basedow case. When she came under investigation there existed a certain degree of exophthalmos. Further Basedow symptoms were lacking, however. The struma was diffuse with small nodules non-pulsating, horseshoe-shaped, slightly constricting. The patient was unexcited, quiet, somewhat phlegmatic, complaining of lack of energy. B. M. −6.6 per cent, after 5 days, calculated again, B. M. was −6.4 per cent. Operated for tracheostenosis. Histological finding: Struma colloides nodosa et diffusa. Chronic thyroiditis. In the tadpole experiment (Case 6 of Branovacky) the thyroid gland was quite active, Basedow-like.

Here we have to deal with a veritable dissociation of symptoms and with a combination of hyper- and hypo-symptoms. Was the case just about to pass from the first to the second stage? Why did the exophthalmos, still not anatomically fixed, have to lag behind? In this instance the assumption of a "mixed dysthyroidism," an inadequate association of secretion components can not be entirely rejected. After a year's time there was still exophthalmos. B. M. −14 per cent. Subjective improvement after treatment with thyroid gland.

8. Adolescent Goiter

In the material thus far reviewed, there are twenty-seven cases of struma from 12-18 years of age and one each of 9, 10 and 11 years. For these last three cases the standard

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values were calculated according to the Benedict determination for somewhat older children and hence the values are only approximate. If we consider these adolescent goiters in the same manner as the collective material, according to their *clinical* aspect, thus we find that

(*a*) For the 15 clinical euthyroid cases, B. M. +0.3 with limiting values of −9.6 and +15.3 per cent.

(*b*) For the 14 cases clinically estimated as hypothyroid, −12 per cent with limit values of +1.3 and −39.8 per cent.

(*c*) For the single Basedow case, +31 per cent.

Hence the average values are similar to those of the total material and we must conclude from this that the fate of incipient goiter cretins is as a rule determined several years *before* puberty.

Concerning the *histological character* of the struma we find in

	Euthyroids	Hypothyroids
Struma colloides diffusa	2	—
Struma colloides nodosa, *i. e.* diffusa and nodosa	—	—
Struma parenchymatosa diffusa	3	1
Struma parenchymatosa nodosa, *i. e.* diffusa and nodosa	1	1
Struma colloides nodosa	—	—
Struma parenchymatosa nodosa	5	9
Mixed forms	2	1
Non-operated: diffuse	1	1
nodular	—	—
mixed	1	—

We find here, too, as in our collective material from the district of Bern, a numerical predominance of struma nodosa parenchymatosa. The mother form of this, the struma parenchymatosa diffusa, in a narrow sense the adolescent goiter, is, indeed, as we must accept from the investigations in the schools, much more prominent, as such, however, it seldom requires operation since it is mostly adaptable to iodin therapy and since it causes tracheal stenosis only exceptionally. It is to be emphasized that there is greater percentage of the purely or predominatingly diffuse forms in euthyroids than in hypothyroids (46 per cent as against 21 per cent) and that in the latter cases the colloid forms do not occur. Lastly, I do not put much stock in the small number of cases. For the study of the early stages of cretin goiters we confine ourselves to the years *before* puberty. We shall touch upon this point again in another place and merely recall the gas metabolism experiments made in our clinic by H. Doubler in 1920-22 on cases of adolescent goiter, which gave the average B. M. of −9 per cent.

(To be continued)

Practical Therapeutics

Sex Gland Therapy

THE endocrine functions of the sex glands are becoming increasingly better understood. In the case of the female sex hormones remarkable additions have been made within the past few years. Potent preparations of both follicular and luteal hormones have been produced and their relation to each other and to the sex hormone of the anterior pituitary in menstruation and pregnancy are beginning to be understood. Likewise in the case of the testicular hormone there has been produced by several groups of research workers active potent and concentrated extracts exerting remarkable biologic effects. The experimental work has demon-

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strated beyond all question the presence of these active sex hormones, both male and female. They may be extracted and produce constant effects. In the case of the ovarian follicular hormone, it has been prepared in crystalline form and shows a potency that is truly astonishing. Both male and female hormones may be given hypodermically or by mouth, and the literature contains sufficient evidence of the clinical value to warrant a much wider use. Novak has outlined a method of treatment using both ovarian hormones that is in accord with the recent research showing the interaction of the follicular and luteal hormone. Whole ovarian substance would now appear to be more promising as a therapeutic agent than purified preparations of either follicular or luteal hormone. Hofbauer (abstract below) outlines the uses of whole ovarian substance. It is worthy of note that Hofbauer, as Graves of Boston has done, emphasizes the use in the menopause. This seems to be a field in which whole ovarian substance is particularly effective. Note Hofbauer states that the preparation should be used "when it contains all the active constituents of the ovary."

The Action of the Sex Gland Hormone on Total Metabolism. — R. Hofbauer. (*Zeitschr. ärztl. Fortb.*, 25: 110, 1928.)

The indications for the use of whole ovarian substance when it contains all the active constituents are:

(1) The treatment of complaints of the menopause. A disappearance of all symptoms is observed: palpitation of the heart, perspiration, dizziness. The women again become vigorous and able to work. The effect of ovarian substance is partly an inhibiting one on the sympathetic.

(2) Treatment of obesity as it may exist in the menopause as well as in young women with lowered sex gland function. Through intensive use of ovarian substance with any diet, a considerable loss in weight may be attained in many cases.

(3) Treatment of Basedow's disease. Here, the lipoid content of the ovary probably acts in so far as it appeases the two strongly acting thyroid hormone and in some measure detoxicates.

(4) Genuine epilepsy, which is of angiospastic nature, is also considerably improved by sex gland preparations.

Therapeutically, tablets as well as injections are recommended.

The authors carried on experiments to determine whether the metabolism and blood pressure are to be influenced by sex gland hormones. He made the observation that all patients felt unusually well following treatment with sex gland extracts. With a food intake of 1700 to 1800 calories daily weight decreases of 12 to 14 pounds were attained on the average within 9 weeks, without any disturbances whatever of the general state of health appearing. In men, the loss of weight in 10 weeks was on the average about 20 pounds, while appetite generally increased. In men as well as in women, a definite fall in blood pressure was obtained. In all probability an antagonism between suprarenals and sex glands plays a rôle here. In any case, a fall in blood pressure of 20 to 30 mm. may be obtained.

THE FAMILY PHYSICIAN

"It has been my good fortune to have intimate knowledge of physicians from childhood—personalities who went by the old and fortunate name of the family physician, the man who was elder brother and counsellor, who was almost as much nurse as doctor, who cared mightily for every patient, who stopped at nothing, whose tenderness matched his skill, and whose devotion went parallel with his service. To have those contacts, to have those memories, to have those relationships is itself a liberal education. That is why I prefer, speaking as a layman and for the patient, to dwell not on the technical aspects of medicine, not any of the new scientific discoveries and methods and possibilities, but upon that larger view which sees the modern physician as the trained man of science and public service, rich in personality, serene and secure in the feeling that others depend upon him, and holding himself for one of the highest and most satisfying services to his kind. The very verb 'to heal' sounds like a benediction."—Nicholas Murray Butler, in Clinical Excerpts.

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The Doctor's Page



GREGOR JOHANN MENDEL

(1822-1884)

Monastery walls have been quite effective not only in secluding the inmates from the whirl of the outside world but also in excluding the prying interest of outsiders as to what is being done within the confines. How much these walls have withheld concerning the life and work of the Augustinian monk and abbot, Gregor Johann Mendel, and how much they are responsible for the concealment of the results of his researches until the re-

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discovery almost twenty years after his death can not be determined definitely. Some service they did render him, however, namely made possible the success of his experimentation and afforded him a position of distinction to augment the value of his work.

Not much is known of Mendel as a man for his intimate letters to the family were few. Women, to whom he might have confided his secret thoughts and ideals were automatically barred by his choice of life. Letters to friends and fellow-workers were all mainly concerned with the work in which he was intensely interested. The letters of the closing years of his life, particularly to his nephews of whom he was very fond, are those of a kindly, peaceful, fatherly advocate; they are attractive bits of composition especially for the wit which formed an element in Mendel's make-up. A short autobiography gives little more than his letters. However, to a resident of Brünn, Hugo Iltis, we are indebted for a splendid accumulation of facts concerning the life and work of Mendel.

Johann Mendel was born in Heinzendorf, in northeastern Moravia, near the union of the German, Polish and Czechoslovakian borders, into a peasant family. From his father he acquired an intense appreciation for the growing things of the earth. His mother instilled in him an aim to a higher social standing. From her he seems to have derived a fine artistic sense. At her instigation he was sent to the gymnasium at Troppau where he showed himself to be a fine student. The cost of enlightenment, however, eventually drained the family resources, and since there were other children in the family to be considered, Mendel was left to seek his own support. His greatest desire was education and therefore, in 1841 he entered the college at Olmnetz; but the efforts expended in acquiring sufficient funds for the undertaking began to exact their toll with the result that Mendel's studies were continually interrupted by breakdowns. After two such years of intermittent study and illness he decided to enter the Augustinian order and as a novice he was given the name Gregor.

He was particularly fortunate in the choice of abbey, for the abbot of Brünn recognized his bent for natural science and encouraged his scientific work and liberal ideas rather than cared for his soul, though, as a result of a series of *faux pas* and too liberal expression Gregor was properly chastised, specifically for having remarked that a "visiting bishop was more distinguished by his fat than by his learning."

Gregor was assigned to assist in the instruction of physics at the Technical High School. His tranquil nature and sly wit made him popular so that eventually the abbot sent him to Vienna to try for a Teacher's Certificate. Gregor failed the examination, it is said mainly because of the antagonism of the board of examiners. The abbot, of course, was displeased, but his faith did not waver. He sent Gregor to the University at Vienna for further preparation. Here the monk seemed to fare well and with the exception of having purchased, so he says, a lottery ticket, he apparently devoted himself solely and diligently to the pursuit of studies. Some time later he again essayed the examination for the certificate, but rumor has it that he returned to Brünn with head wrapped in bandages, a hazy recollection of having been in Vienna, but no teacher's certificate. In fact, he never obtained it.

At the convent Mendel spent much time in the laboratory in which he kept birds, mice, a fox, and a porcupine. In the garden he kept bees, grew flowers and shrubs in profusion and in a hot house, such unusual fruit as the pineapple. These growing things he referred to as his children, indeed he cared for and nourished them beyond imagination. Besides his experiments and instructive occupation, reading occupied much of Mendel's time. Darwin's books, of course, were forbidden to good catholics, but this free-thinker, in some way, managed to procure them and read them with profound consideration. He was also attracted to the study of astrology and for years, even up to the close of his life, he kept a meteorological record.

In 1868 Mendel was elected abbot of Brünn. He then gave full sway to his experimental bent. Things grew in profusion all over the laboratory. The garden was greatly increased and became a veritable paradise of sweet-smelling and rare blooms. He also indulged in a life of ease and good eating, entertaining guests much after the fashion of the abbots of former days, for he was a lavish host.

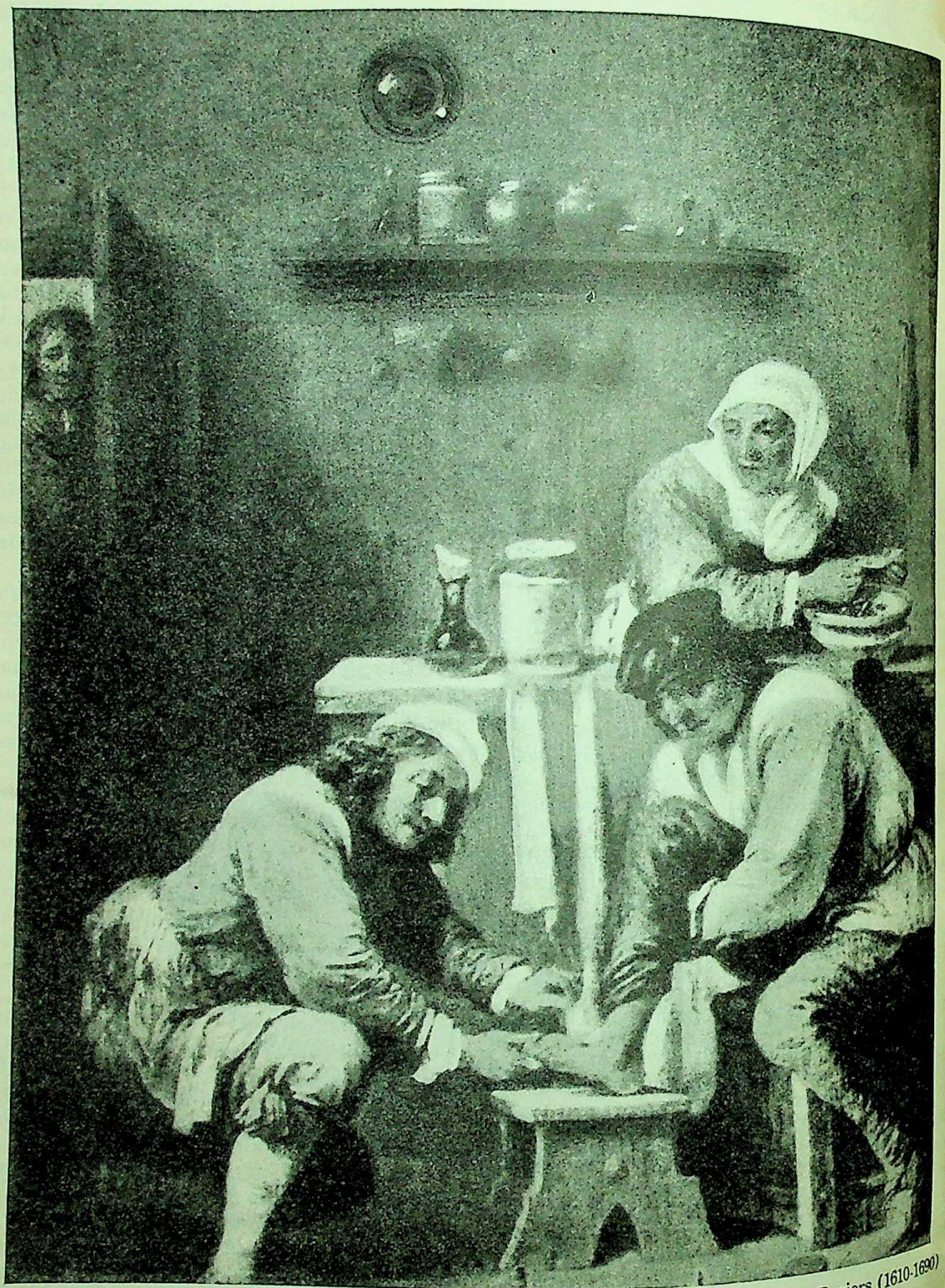
The experiments of this unusual cleric scientist were always shrouded in mystery, which was the source of comment and discontent among both associate monks and laity. As time went on there occurred several

(*Continued on page 307*)

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Medical Subjects by Famous Masters



"A BARBER SURGEON REMOVING A PLASTER FROM A MAN'S FOOT," by David Teniers (1610-1690)
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Editorial Comment

The Journal of Organotherapy

A Journal for Physicians

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Pituitary Extract and Its Influence on the Intestine

THE use of pituitary solution in acute atony of the stomach is described by Königsberger and Mansbacher (abstract below). With injection of 0.5 to 1 cc. they essen the period of chyme retention in the tonic stomach. This effect is lacking in the stomach with normal tonus.

The earlier reports of the action of post-pituitary solution on the intestine agreed as to its stimulating influence resulting in definite contraction. Thus, injection into rabbits induced defecation and strong peristaltic movements. Intestinal strips bathed in a solution of post pituitary showed contraction and it was believed that the post-pituitary principles exerted a direct effect on the unstriped muscle.

Subsequent research on the subject, however, resulted in some apparent contradictions of the conclusion on which the earlier investigations had been practically unanimous. Under some conditions decreased tonus and lessened contraction were reported. The pre-existing conditions of tonus and the preliminary action of certain drugs seemed to modify the result. Other investigators reported a preliminary decrease in tonus followed by a decided increase of tonus and peristaltic movements. Some observers have demonstrated quite opposed effects of strong or weak solutions, and a marked dependence on the degree of tonus present in the muscle at the time. The effect of post-pituitary solution also seems to vary in different parts of the alimentary tract. In Königsberger and Mansbacher's article a report is made of stimulation of tonus and contraction in an *atonic* stomach. This seems to be consonant with recent work showing the dependence of the effect of existing tonus. X-ray studies of the effect of post pituitary on the stomach have also shown a primary depressing influence upon peristaltic movement and motility followed by an increase in both.

The clinical use of post-pituitary solutions in ileus, intestinal paralysis, atony, etc. needs further study before it becomes the effective agent that its action suggests.

Therapeutic Investigations with Pituitary in Atony of the Stomach in Nurslings and Young Children. — E. Königsberger and W. Mansbacher. (*Zeitschr. Kinderheilk.*, **44** : 1929.)

In acute atony of the stomach an abbreviation of the length of retention of chyme in the stomach may be obtained with an injection of 0.5 to 1 cc. of hypophysin. In normal tonus of the stomach this effect is lacking. By means of a combination with 0.0003 gm. atropin or the less reliable adrenalin (0.0003) the hypophysin effect is intensified. Clinically, after administration of the combination in severe acute atony of the stomach an abrupt cessation of vomiting was to be observed. The former hunger cure, which was undertaken for the evacuation of the stomach is hence superfluous.

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Abstracts

Malignancy of the Thyroid. — Norris W. Gillette. (*Am. J. Surg.*, **2** : 556, June, 1927.)

Carcinoma occurs in about 3 per cent of all cases of thyroid resections. Patients have a good chance of recovery if the diagnosis of malignancy is made by the pathologist and not by the surgeon, *i. e.* postoperatively. Metastases of the thyroid are of thyroid type cells developing thyrotoxicosis.

A nodular gland is surgical and early removal will save many from death from carcinoma. Extension is early by way of the blood vessels, later direct and by lymphatics. There is no such thing as benign metastases of thyroid gland.

Insulin Edema. — I. M. Rabinowitch. (*Canad. Med. Assn. J.*, **17** : 685, June, 1927.)

Insulin produces an edema of the body tissues of the diabetic person, and this largely accounts, in a great number of cases, for the rapid increases of body weight so frequently noted. The recognition of this phenomenon is important in order to estimate properly the progress in a case of severe diabetes. The proof that the rapid gains of body weight are due to a large extent to water retention is the fact that, as the insulin is discontinued, polyuria occurs, and approximately parallels the loss of body weight. Hyperglycemia gradually increases during the first few days after the insulin is discontinued but glycosuria is frequently absent. The polyuria thus differs from that of active diabetes. Obviously, if the insulin is discontinued for a certain period, the diabetes becomes active, and glycosuria reappears. Following institution of insulin treatment, without alteration of food or fluid intake, the polyuria disappears, and the patients again begin to gain weight. Rabinowitch reports two cases as typical illustrations of this phenomenon.

Insulin edema may, at times, be harmful, in view of Joslin's suggestion that it may be a factor in the production of the anuria which develops during coma. It is interesting to note that just as a suggestive relationship between insulin dosage and edema is found, so Joslin finds such a relationship between insulin dosage and anuria.

Encephalitis Lethargica. — George Riddoch. (*Brit. Med. J.*, No. 3481 : 537, Sept. 24, 1927.)

Encephalitis lethargica is essentially a chronic disease. One never knows when the patient is cured. In the late stages of the disease endocrine disorders are frequently met with. Adiposity, with or without disturbance of the sexual functions, is by no means uncommon. Duncan found it in 7 out of 83 cases. One of the author's patients, a young girl, who became rapidly and grossly fat after an acute attack of the disease, had amenorrhea lasting for many months. Later she developed exophthalmic goiter, and her weight diminished, but did not fall to normal until she made an apparently complete recovery in 18 months. In another case tachycardia, tremor, slight goiter, and emotional instability appeared in a girl a few weeks after she had seemed to recover from the acute phase of her illness, and persisted for many months. Diabetes insipidus and glycosuria are also occasional late results of the disease.

Ovarian Hormone in a Water-Soluble Form. — F. Dickens, E. C. Dodds, and D. J. Trescott Brinkworth. (*Lancet*, **212** : 1015, May 14, 1927.)

A method is described for obtaining the estrus-producing hormone in a water-soluble form by extraction from placenta, the yield being over 1000 rat units per kg. The activity of the preparation can be easily reduced to below 0.5 mg. per rat unit. Further work indicates that this degree of purity may be exceeded without much difficulty.

The product obtained is a pure white powder very soluble in water. It can be boiled in aqueous solution for a considerable period without loss of activity. The active principle passes completely through a collodion mem-

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brane, and the substance may be purified to some extent by this means. The chemical constitution is being investigated. The substance appears to be relatively simple and contains a fairly large proportion of sulphur. The Pauly reaction for histidine is strongly positive. Tryptophane also appears to be present.

Thyrotoxicosis and Associated Vagotonic and Sympathicotonic Syndromes.—Virgil E. Simpson. (*Am. J. Surg.*, **3** : 249, Sept., 1927.)

Since the symptomatology of a toxic thyroid is so closely linked to the sympathetic nervous system it would appear that the line of cleavage between vagotonia and sympathicotonia drawn by Eppinger and Hess would have an intensely practical value. Lack of uniformity, however, in designation of these two divisions of the autonomic system has added to a confusion already existing based on an anatomical separation difficulty. Langley's pronouncement is, probably, as workable as any other. According to him the autonomic system embraces the entire sympathetic nervous system and is divided into: (*a*) The sympathetic autonomic, including certain fibers of the vagus nerve. (*b*) The vagal autonomic. Under the first grouping are placed all the nerves that pass through the ganglionated cord, and in the second, the remaining vegetative fibers or expanded vagus. The ganglionated cord referred to, also called the trunk, passes parallel to, and in front of, the vertebral column and presents a corresponding ganglion for each vertebral segment. The autonomic system is also called the vegetative nervous system and may be visualized as an outgrowth of the cerebrospinal system. This nomenclature would seem simple and sufficient, but the perplexity lies in a manifest lack of agreement in designating the same thing by the same name.

The vegetative system may be divided anatomically into two units. One is composed of fibers originating in the middle portion of the thoracic and the upper lumbar cord which pass through the ganglionated cord after which many become mixed with other fibers and their identification where they terminate as end organs becomes difficult or impossible. The fibers of the other unit have their origin in the brain, the medulla

(*Continued on page 284*)

A Gynecologist's Opinion

"Functional amenorrhoea—the amenorrhoea or oligomenorrhoea that is seen in fully developed women, who have previously menstruated normally, is accounted for as a result of functional ovarian deficiency, a theory that finds strong confirmation in the almost immediate beneficial effect which ovarian extract usually has on these cases." (*Gynecology*---Graves)

The ovarian deficiency may be due to deficiency of the anterior pituitary the "motor of the ovary." Prescribe

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and the sacral segment of the cord and do not have a relation to the ganglionated cord.

The physiological facts are more uniformly agreed upon. The vegetative organs have a dual nerve supply which is antagonistic. This double innervation of these organs not under the control of the will is of tremendous importance, and this mutually antagonistic arrangement maintains a balance in function which is indispensably protective. However, the physiological process though it appears simple is influenced by the endocrines. The secretions of these glands exert a powerful effect on the mechanism of body metabolism. The action, so far as known, of the endocrine secretions on metabolism would seem to justify grouping them into those (*a*) activating, and those (*b*) inhibiting it. In the first group may be placed the thyroid, suprarenal and pituitary glands while in the second group would be found the thymus, pancreas and parathyroid glands. This relationship to metabolism covers proteins, fats, carbohydrates and mineral substances. Whenever the balance between the sympathetic and vagal autonomic divisions which exists normally is disturbed one or the other obtains the ascendency. Certain of the endocrine hormones act through the vagal division alone while others act through the sympathetic and yet others act through both. The adrenals are active, powerful sympathicotonic agents while the pancreas exercises an equally selective effect on the vagal division. Thyroid secretion expresses itself through both, hence, the hypothyroid patient is not purely vagotonic nor is the hyperthyroid victim purely sympathicotonic.

Viewed clinically, vagotonia appears to be a chronic state of vagal excitability and the organs supplied by this system will be found to be in a state of irritability. Recalling the structures receiving their nerve supply through the vagal system, the symptoms of vagotonia become a matter of multiplied physiological action. Through it the gastric and pancreatic secretions are increased, peristalsis reinforced, the heart slowed, Zinn's zone relaxed and the pupil contracted.

Sympathicotonia is practically a normal condition in females and though occurring in a fairly large percentage of males it should be looked upon in men as a stigma of feminism. Its anatomical as well as physiological anomalies occur chiefly in the nervous cardiovascular system. Neuropaths and psychopaths are common in this group, likewise neurasthenia finds plentiful recruits in these unstable nervous individuals. The author gives a grouping of the symptoms of vagotonia and also of sympathicotonia. Charts showing vagal and sympathetic predominance in thyrotoxicosis are also given.

While the manifestations attributable to either the vagotonic or sympathicotonic group may be kept in mind, yet they will be disconnected.

Acromegaly. — Harvey Cushing. (*Brit. Med. J.*, No. 3470 : 48, July 9, 1927.)

The surgeon before operating in cases of acromegaly must seriously take into consideration the influencing by operation of the secondary effects of hyperpituitarism. Serious consequences ensue upon damage to the hypothalamic center. It is a region to be shunned lest diabetes insipidus, excessive adiposity, and even a fatal cachexia supervene. Evans and Smith by their work have shown that the hypophysis is primarily concerned with growth. No less definitely do their experiments show that it is an activator of the reproductive organs. Nature has provided that neither the pathological giant nor dwarf should reproduce his kind. These states, which necessarily originate in preadolescence, are represented by corresponding ones which set in later in life when normal skeletal growth has been attained. In these circumstances, too, for different causes apparently in the counterposed states of hypophyseal overaction and underaction, the functions essential to reproduction are interfered with. But this is only the beginning of a long sequence of alterations in other glands, affecting the thyroid and pancreatic islets in ways but partly understood, the parathyroids, adrenal cortex, and the rest in ways not understood. Then there are the final stages in the two conditions of glandular insufficiency and overactivity; on the one hand the tissue atrophy with resultant senility and cachexia; on the other hand, splanchnomegaly and tissue hypertrophies are produced which, as in the case of the heart, lead to equally dire consequences. Not until some practical form of substitution therapy is at the surgeon's call will he properly run the risk of overdoing his extirpation, for a daily homoplastic transplant so strikingly effective in the hypopituitary rat is out of his reach.

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The Pancreas Hormone of the Unborn Child. — Holzbach. (*Zentr. Gynäkol.*, **53** : 1907, 1929.)

Examples of the presence of fetal insulin are presented from

1. The anatomical structure: the incretion-producing island apparatus in the newborn is about four times more powerful than in the adult. In the embryo it is developed much earlier than the excretory parenchym.

2. The physiological confirmation of the activity of fetal island apparatus producing the incretion is brought out by the fact that the ferment-free pancreas of ox fetus was given as an insulin restorative. By means of refinement of method (mouse test) the active incretion is also to be observed in the human fetus. The author has found it in human fetuses of all ages, beginning with a fetus 21½ gm. in weight. In dry weight, *i. e.* derived from 1 gm. of pancreas, the fetal pancreas exceeds the adult pancreas many times in insulin content. By means of animal test and clinical observation the fact is definitely determined that the blood of the mother passes through the placenta with a slight loss of sugar content, however, it experiences an effective exhausting of blood sugar in the fetal organism. The author presented the assumption that this exhaustion is executed by means of a pancreas incretion in the fetal body, following his observation on diabetics who were pregnant. Through the work of Laqueur it was shown that the female sex hormone is not so strongly antidiabetic that it can depress the heightened blood sugar content of pregnant diabetics to normal.

On the Question of Endocrine-Toxic Epilepsy (Serejski). — E. N. Krylowa. (*Zeitschr. ges. Neurol. u. Psychol.*, **121** : 521, 1929.)

The importance of the endocrine organs for the pathology of epilepsy according to Redlich, are shown to be most convincing if it is possible, by means of an arrangement of one or more organ preparations, to obtain a specific therapeutic effect in epilepsy. The author studied three cases of epilepsy under endocrine treatment, in two cases hyperthyrosis and in one case ovarian insufficiency were demonstrated.

In both of the former cases the Lugol treatment and in the third patient the administration of ovarian preparations led to extensive improvement and a reinstitution of the working capacity. In the determination of the syndrome of endocrine-toxic epilepsy the author sees a new means of prognosis and therapy of a certain number of cases which were previously held to be hopeless.

Uterine Movements and Maturation of the Ovum. — Kok and Seel. (*Klin. Wochenschr.*, 8 : 1265, 1929.)

The normal physiological movements of the uterus in the animal are stronger at the time of estrus than in the inter-estrus, in the tubes the opposite was found. Adrenalin makes it possible for these movements to increase. In the uterus of the hog there is no synchronism, the change occurs more in the topographical-anatomical course, from within out.

On the Physiology of Corpus Luteum. — Hermann Knaus. (*Arch. Gynäkol.*, **138** : 201, 1929.)

As the investigation of the author shows, the corpus luteum of rabbits suppresses, in hormonal manner, the maturation of follicles and ovulation. The opinion held by many sides that the corpus luteum, the ovary and the placenta form a unit is incorrect. Only a common property occurs in these three different substances, namely to call forth estrous symptoms in the castrated mouse.

Concerning the Relationship between Sexual Hormone and Hormone of the Anterior Lobe of the Pituitary and Lipoid Tolerance in Human Beings. — Carl Kaufmann. (*Zentr. Gynäkol.*, **53** : 1904, 1929.)

Investigations on thirty-seven women concerning the action of the ovarian hormone and the hormone of the anterior lobe of the pituitary on the amounts of cholesterin in the blood gave the following: During the course of a treatment by injection and also after per oral administration of large doses of the sex hormone "folliculin" a rise of cholesterin in the blood is demonstrable, which abates again with cessation of administration of the hormone. In contrast to the investigations of Reiss and Langendorf it was impossible for the author to obtain in human beings by means of injection of the hormone of the anterior lobe of the pituitary a lasting increase of cholesterin in the blood, such as occurs after treatment with ovarian hormone. Also,

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after per oral administration in doses up to 6800 rat units given to one patient, permanent rise in cholesterin remained indiscernible. Rather, in a large majority of women a characteristic change of blood cholesterin content was observable shortly after the injection. The effect of the ovarian hormone on the cholesterin content appears to be a specific hormone effect, while the action of the hormone of the anterior lobe of the pituitary as a stimulating effect must not be excluded entirely.

Therapeutic Investigations with a Certain Fraction of the Posterior Lobe of the Pituitary in Diabetes Insipidus Including Observations on Its Mechanism of Action. — S. Isaac and R. Siegel. (*Klin. Wochenschr.*, 8 : 1700, 1929.)

E. Frank, the discoverer of the relationship between disturbances of the pituitary and diabetes insipidus, has recently sought to substantiate the pituitary theory of this disease against the theory of other research workers who agree that the pituitary plays a part in the pathogenesis of diabetes insipidus and assume a localized nerve center for the water diuresis in the tuber cinereum, injury to which would result in excess excretion of urine. With regard to the value of previous experimental material which has been gathered for the support of this point of view a report is made in the contribution of Frank. Here it suffices to say that since the fact was discovered by R. v. D. Velden, of a curative effect of injections of extract of the posterior lobe of the pituitary in diabetes insipidus, numerous bits of information for a hormonal regulation of the kidney function by means of the pituitary have been brought out. Quite in this sense, also, P. Trendelenburg has recently worked on the investigation. He found that after extirpation of the pituitary there was a substance in the tuber cinereum which had the same effect as the extract of the posterior lobe for inhibiting diuresis and excretion of salt. It is present only in small quantities in the tuber cinereum of normal animals. When the urine-inhibiting substance first arises after extirpation of the posterior lobe, a vicarious formation of hormone occurs in the tuber cinereum. This finding explains all the contradictory reports of experimental research up to the present time and is a strong support for the hormone theory.

Most of the pituitary preparations used for a long time passed, such as hypophysin, pituglandol and pituitrin, are extracts of the posterior lobe which have a known effect on the smooth musculature of the uterus, the liver and the blood vessels as well as a restricting action on diuresis. Many failures in the therapy of diabetes insipidus are perhaps to be traced back to the fact that the dose offsetting the disturbance of water and salt metabolism is not sufficient to bring about the strong action on the uterus or liver musculature and hence the administration of the amount adequate for diuresis inhibition in the course of time is incapable.

Previously Oliver Kamm and his colleague worked on the problem. It was possible for him to isolate two different substances from the posterior lobe of the pituitary: the first worked only on the uterus and the second tonicized the blood vessels and intestinal musculature and inhibited the diuresis, particularly the pathological.

In the following the authors reported likewise on two special fractionated preparations derived from the posterior lobe of the pituitary. The one has, besides the effect on the blood pressure and on the musculature of the intestine, a strong diuresis-inhibiting effect which could be determined; the other acts only on the uterus musculature.

From the investigations of the authors it was shown that in hypochloremic diabetes insipidus the pressor hormone restrains the excretion of water, causes the thirst to disappear and increases the concentration capacity of the kidney for salt. Further, the reduced salt content of the blood is restored to normal. Hence, the genuine diabetes insipidus was a hormonal disease, while in the hyperchloremic cases, associated with disturbance of tissues, a central neurogeneous component was to be acceded. It is comprehensible that an intense over-supply of pituitary hormone also makes possible the remedy of the tissue disturbance; hence the water and salt metabolism ostensibly very important for the determination of the life processes is doubly assured, *i. e.*, it is regulated hormonally as well as by the nervous system.

Considered impartially, in the organism, the facilitated mobilization of salt out of the tissues and the increased capacity of the kidney for excretion of the latter, by which this takes effect with the least possible loss of water for the body, appears the essential one

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of the combined effects of the hormone of the posterior lobe of the pituitary. (Dissociation of water and salt diuresis.)

Contribution to the Study of Icterus Catarrhalis and the Treatment of It. — J. Pavel, C. Bratesco and G. Negresco. (*Arch. mal. appar. digest. et mal. nutrit.*, **19** : 696, 1929.)

The author has given insulin for the treatment of hepatitis patients. Although the insulin treatment of this disease form has been revived repeatedly, the majority of the clinicians have attributed it to various causes. Besides the insulin the author gave simultaneously sugar perorally or glucose rectally. In spite of the good effects of insulin the author, however, saw disagreeable attacks.

Concerning the Modern Medical Therapy of Diseases of the Bile Duct. — Ferdinand Lebermann. (*Med. Welt*, **3** : 1077, 1929.)

The most modern procedure for therapy of diseases of the liver and bile is treatment with sugar and simultaneous administration of insulin. It should incur the retention of glucoses in the liver and hence forestall the imminent injuries due to glucose impoverization. Very good results have been reported by many authors with this insulin-sugar cure in accordance with the procedure of P. F. Richter and Umber.

Biology and Clinic of Sleep. — Poetzl. (*Jahreskurse ärztl. Fortb.*, **20** : 6, 1929.)

Cushing and Goetsch have demonstrated involution symptoms of the pituitary in the winter sleep in animals and refer this condition to changes in pituitary secretion (anterior lobe). Adler was able to determine experimentally that the hedgehog in winter sleep, could be awakened by a subcutaneous injection of thyroid gland extract. This confirms the hormone dependency of winter sleep. Thymus extract, adrenalin and anterior lobe of the pituitary have the same effect. Adler describes the winter sleep as a result of hypofunction of the thyroid, evidently also of the pituitary and suprarenals.

Salmon has presented a hormonal hypothesis for normal sleep. The detoxication of the toxin of fatigue proceeds through the activity of the endocrine glands. When these function poorly, eventually sleeplessness occurs. According to Mingazzini and Barbara the hormones of the thyroid, the suprarenals, the genitals and the hypophysis exercise a promoting action during the waking hours. In sleep, however, "the hormone acting anabolically on the tonus of the autonomic system" would come into effect.

Genital Hemorrhages in Young Girls. — F. Kermauner. (*Arztl. Praxis*, **3** : 235, 1929.)

One is inclined today to assume a disturbance in the coordination of the incretion organs in rather obscure cases. There are many examples known of this. There are girls with intense hypothyroidism and genital hemorrhages. Administration of thyroid gland sets this in order in a short time. Besides the older remedies the author is inclined to give pituitary preparations as coagulant medium. Likewise in pronounced hypoplasia ovarian preparations, but only the best and most active and only for a short time.

Contribution to Thyroxin Treatment of Congenital Myxedema. — Nobel and Kornfeld. (*Zeitschr. Kinderheilk.*, **48** : 216, 1929.)

The authors report on a 17 year old girl previously untreated, with severe congenital myxedema, in whom after 1½ years of continuous thyroxin treatment an increase of body growth up to 18 cm. and a quite complete reconciliation of the former high degree of retarded ossification could be obtained. The changes in the soft parts to effect the reconstruction are particularly rapid, while the mental development in less satisfactory manner derives from the thyroxin treatment only what is to be expected from an all too long life period without treatment, in exhausted athyrotic state.

Endocrine Pancreas Therapy in Chronic Venous Disturbances and Their Complications. — Pierre Quiserne. (*Paris med.*, **19** : 156, 1929.)

The treatment of varicose ulcers by means of local insulin application in the form of salve or ointment, gives quite varied results. In one case prompt cicatrization of the varicose ulcers was obtained, in other cases the treatment remained ineffective.

The author treated experimentally with insulin injection patients who suffered from Claudicatio intermittens, and obtained satis-

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factory results therewith. The influence on the trophic disturbances of the skin obtained by this method of treatment was striking. This observation led to the investigation of peroral dosage of total substance of the pancreas gland. This method of treatment far surpassed the insulin injection method, as well regarding spasmodic vasomotor disturbance of the Claudication as the trophic disturbances of the skin and other tissues. This last was corroborated by use of peroral gland administration in patients with varicose ulcers. The skin lost its infiltrated appearance, was again supple and acquired also an approximately normal color. Even the pigmentation in several cases showed a definite involution. There is no doubt that pancreas treatment in these cases had good results; also it seems that the administration of other endocrine gland substances along with the pancreas, augment the effect of the latter or activate it. In this sense, indeed, the parathyroid substance is to be regarded as an adjuvant. The same holds true in the internal application of ovarian and testicular substances in varicose ulcers. The pancreas substance itself, through its anti-spasmodic effect, on the vasomotor, seems to have a favorable influence on the painfulness of this form of disease.

Studies on the Cardiovascular Effects of Insulin. — Carl-Eric Räihä. (*Skandinav. Arch. Physiol.*, **57** : 243, 1929.)

From the author's experiments it was shown that:

1. After intravenous injection of insulin the volume per minute of the heart is decreased. The slight degree of decrease lasted for a time.
2. After an intravenous injection of insulin the blood pressure in the aorta falls for a time (about 10 to 30 minutes).
3. Directly following an insulin injection the blood pressure in the Art. pulmonalis is raised; later a depression of the pulmonalis pressure occurs which, in most cases, again passes to a blood pressure increase.
4. After an insulin injection the vagus-stimulating effect on the heart decreases to a greater or less degree. This decrease of effect of vagus stimulation as a rule was raised for a time after the administration of a subsequent adrenalin injection. During the increased pressure state caused by adrenalin the effect on the heart of the vagus stimulation is greatly offset.

The Physician's Interest Is a Human Interest

The primary concern of the physician lies in the welfare of the patient. The laboratory and research workers have special problems and phases of a disease process uppermost in their mind.

The physician in practice is treating a patient and he is attempting to restore the health and well being rather than to influence particular phases of the disease affecting his patient.

It is possible to favorably influence the entire diabetic process; increase the strength of the patient; favor the regeneration of the defective pancreas; modify the disturbed carbohydrate metabolism.

These effects are possible with Trypsogen which contains not a single pancreatic hormone affecting a single phase of diabetes, but a number of internal pancreatic secretions necessary (as shown by experiment) for maintenance of normal health and the enzymes which are lacking in diabetes.

This is a treatment of the patient shown by practical clinical experience to curtail or modify the diabetes, and gradually to promote a restoration to normal. Diabetes is a chronic disease and is not subject to quick treatment or recovery.

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Therapeutic Investigations with Liver in Schizophrenic Diseases. — Eugen Rakonitz. (*Monatsschr. Psychiat. u. Neurol.*, **73** : 116, 1929.)

An under-cooked preparation was administered, which had been given in pernicious anemia with successful consequences. The preparation had the drawback of not being injectible and hence incited aversion as does every intense feeding of liver after a time.

The duration of feeding was 30 to 50 days. Five paranoids, seven cases of dementia simplex, five hebephrenes, two catatoniacs and three stuporeses were treated. The body weight of the patient increased in twelve cases during treatment. The formation of blood showed a tendency to recover in seven anemics. Digestive disorders were not released through the treatment. In those patients with depressed spirits the temperament was improved. In many cases the general condition was improved. There was no observation to portend the fact that liver treatment, as substitution therapy has any specific effect. With the preparations used, the behavior was similar to that with hormone preparations in general. It is not known what they contain. However, substitution therapy remains for the time being, the only conceivable method of investigation.

Clinic and Therapy of Hemorrhages in Puberty. — H. Runge. (*Zentr. Gynäkol.*, 53 : 2252, 1929.)

Curtailing operations and castration must be avoided in all cases. In isolated cases improvement ensued after injection of pituitary extract and suprarenin, other cases reacted well to insulin. However, it is possible only in a few cases to avoid relapse from the beginning. Treatments with ovarian hormone preparations are contraindicated in glandular cystic hyperplasia of the mucous membrane of adolescents, since the investigations at the Kiel Clinic have shown that the hormone status in glandular cystic hyperplasia is raised above normal.

On the Liver Therapy of Pernicious Anemia. Continued Observations on Twenty-Five Perniciosa Patients Treated with Liver. — Hans Schulten. (*Münch. med. Wochenschr.*, **76** : 1281, 1929.)

Twenty-five patients were observed continuously for 2 to 3 years. Liver therapy is not only the best medium against blood changes of perniciosa, but it is also, mainly, the most secure method of treatment, and it is a mistake not to give it. In the medical polyclinic of Hamburg University (resident division) liver extract in amounts of 40 to 100 cc. corresponding to 250 to 600 gm. fresh liver was given. In most cases 20 to 40 cc. were sufficient for the support of the therapy. The proposition may be offered that practically no relapse occurs with adequate liver therapy. Indeed, even with deficient or inadequate liver administration a remission may be warded off for a long time. In each case it may be said that the prospects of liver therapy for perniciosa patients have been greatly improved by means of liver therapy.

The Influence of Hormones on the Sugar Distribution and Cell Permeability in the Animal Organism. — Rudolf Siegel. (*Klin. Wochenschr.*, **8** : 1659, 1929.)

From the exhaustive investigations of the author it is shown that under physiological conditions insulin promotes sugar deposit and glycogen fixation in the liver, in the musculature it raises the infiltration capacity of sugar and raises the conversion of this into glycogen under simultaneous oxidation of an insignificant portion. In very low concentration adrenalin, under physiological circumstances, acts in the same manner as insulin, namely glycogen-fixating. In the body periphery it is its antagonist insofar as it restricts coincidently the recurrence of blood sugar in the musculature. In cases of glycogen impoverization adrenalin excites the liver by furthering the formation of lactic acid from muscle glycogen to a new formation of liver glycogen. Adrenalin is almost without effect on the oxidative sugar metabolism of carbohydrate. Only in abnormally high concentration (shock, experiment) did adrenalin act in an opposite sense, glycogen saccharification by stimulation of the sympathetic terminal in the liver. In thyroxin, however, we must perceive the real antagonist of insulin and adrenalin in the liver, while in the body periphery a direct influence on the carbohydrate metabolism under thyroxin was not to be demonstrated.

For the maintenance of normal carbohydrate metabolism the harmonious alternate play of the individual incretions is of greatest importance. The way in which disturbances of the hormone equilibrium under pathologi-

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cal conditions act, for example in diabetes mellitus, will be reported in another communication.

New Contributions to Our Hormone Studies. — Siebke. (*Klin. Wochenschr.*, **8** : 1644, 1929.)

Siebke uses the hormone prepared by him therapeutically for stimulation. The preparation was put through a Berkefeld filter in highly concentrated solution, and by means of 2‰ tricresol is preserved in ampoules. No evidences of irritation are to be found after injection. The content of the solution in mouse units is constant the month long, up to the present. Sexual hormone: Quantitative investigations (method of Laqueur) on the amount of sexual hormone in the urine of women, outside of pregnancy, gave evidence that the entire amount excreted during a cycle (from beginning of a menstruation up to the next menstruation) varies between 250-1000 to over 2000 mouse units (!). In venous blood at the most there is found from 1 unit to about 7 the third day after menstruation in 25 to 40 cc. In accordance with Laqueur's plan for every cure about 10,000 mouse units of ovarian hormone would be given in dragées. (Commencement of the cure 12 days before the expected or desired menstruation, increasing amounts, sudden cessation after maximal doses.) Good and in some cases very good results were obtained in proper indication. Corpus luteum hormone is lacking in metropathia hemorrhagica (histological glandular cystic hyperplasia). The sexual hormone, corresponding to the persistence of the follicle is demonstrable in high concentration in venous blood until well into the time of bleeding.

A Stimulation Substance of the Central Organ and the Central Function. — E. Steinach, partly collaborated by H. Kun. (*Med. Klin.*, **25** : 1221, 1929.)

On the basis of experimentation the author comes to the conclusion that the problem of incretory function of the central organ is elucidated and the experimental basis for a relative hormone investigation is given. From the brain the author derived a stimulation substance which is obtainable in large quantities from the brain cortex substance and which may be identical with the hormone of the anterior lobe of the pituitary. Doubtless there are relations or correlations between the brain stimulation substance and other incretions. Perhaps it will follow that diseased conditions of the central nervous system and psychic anomalies are based upon a lack of or a defectiveness of the stimulation substance. In all such cases therapeutic application can be assigned.

The Influence of the Endocrine Glands on the Healing of Diseases. — A. Theilhaber. (*Münch. med. Wochenschr.*, **76** : 1241, 1929.)

The author presents the suppositions that the panhormone in many diseases is more necessary than the pure hormone, the intact living substance more active than that injured or destroyed in the factory, the whole organ more necessary than the extract. An instituted tissue depot in the sick body acts better than injection repeated several times weekly, and by oral application many valuable substances are indeed destroyed by the juice of the digestive canal.

Implantation effects a powerful increase of all the living processes of the organism, in amenorrhea menstruation is often recommenced. In twenty-six patients with disorders of the central nervous system (spinal anterior poliomyelitis, multiple sclerosis, syringomyelia, encephalitis, etc.) the author has treated them with implantations of spleen, thymus, thyroid gland and liver and gained improvements in some and in one case, cure. Likewise the struggle of old age and the diseases of old age is resumed by this method. The stimulation of the hormone is a very important factor for the growth of the organ. Thus, in infancy, for example, if the hormone of the ovary is lacking the uterus is underdeveloped. If the hormone of the ovary is again decreased *post climacterium*, the uterus atrophies. The activity of the organ to be implanted is augmented by treatment of the animal from which it is taken. The administration of endocrine gland substances prophylactically in various diseases and of gland extracts in premature senility is desirable.

Influence of Pituitrin-Snuff Powder in Severe Diabetes Insipidus. — Schalscha. (*Münch. med. Wochenschr.*, **76** : 1491, 1929.)

The author reports on the therapeutic investigation, particularly bringing out the good results effected by pituitrin in endonasal application, while it proved ineffective with *per os* administration.

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Studies on the Biology of the Placenta of the Guinea Pig. — Vilardell. (*Gynécol. et obstet.*, **20** : 65, 1929.)

Extract of fresh guinea pig placenta after intraperitoneal or intracardial injection, causes a chlorosis and unimportant changes in the kidneys and liver of other guinea pigs.

The placenta autolysate after intraperitoneal or intracardial injection causes anemia perniciosa and alterations in the kidneys and liver of other guinea pigs.

Extract of fresh guinea pig placenta possesses, when injected intraperitoneally into other guinea pigs, an anti-glycosuric action.

The author believes that the placenta of the guinea pig has a hormone effect which is stimulating on the pancreas and inhibiting on the suprarenals and thyroid gland.

Concerning Temporary Hormone Sterilization of the Female Animal by Means of Feeding Insulin. — E. Vogt. (*Med. Klin.*, **25** : 1163, 1929.)

From investigations on mice it was shown that: The temporary hormone sterilization of female animals may be obtained in the same way by feeding insulin as by parenteral administration. Hence a new fact is brought out, that insulin, at least as far as its sterilizing effect is concerned, also displays this effect in resorption from the intestinal tract.

In the fact that the female sex hormone in the form of a pure preparation of folliculin, when administered *per os*, acts in animal experiments as well as clinically, and that mice can be temporarily sterilized by feeding of insulin without the occurrence of general damages, the author sees a confirmation of his previously obtained information, that the pancreas hormone, the ovarian and the placenta hormones, or the female sex hormone, are closely allied with one another and above all display themselves in this sterilization characteristic.

Concerning the Diagnosis of Pregnancy from the Urine by the Presence of the Hormone of the Anterior Lobe of the Pituitary. — E. Vogt. (*Münch. med. Wochenschr.*, **76** : 1401, 1929.)

The method of demonstrating the hormone of the anterior lobe of the pituitary in the urine of pregnant women is a method free from objection, and technically comparatively simple, for the diagnosis of early pregnancy. The author describes the working out of the new method for clinical-therapeutic investigation by implantation of anterior lobe of the pituitary from animals and through parenteral administration of a pure hormone of the anterior lobe of the pituitary, according to the practical contribution of Zondek and Biedl.

On the Diagnosis and Therapy of Disturbances of the Pituitary. — Wiele. (*Münch. med. Wochenschr.*, **76** : 1491, 1929.)

Diabetes insipidus is to be treated with extract of the posterior lobe, parenterally, primary oliguria, however, is not definitely influenced. Simmond's disease, correctly diagnosed, can be affected with substitution therapy. Disturbances of growth with pituitary symptoms likewise give good results under substitution therapy eventually combined with substances of other glands. The condition of the pituitary dwarf can be influenced best.

Concerning the Clinical Significance of the So-Called Heart Hormone Preparation. — Max Winternitz. (*Med. Klin.*, **25** : 1218, 1929.)

According to the observations in the clinic of Professor R. Schmidt it was shown that cardiac hormone extracted from the ox heart according to Haberlandt is effective in anginoid symptoms as well as in the attack, prophylactically. According to the indication of the patients treated, nitrite is incorporated for the permanence of the effect and prophylactically. The action apparently takes effect by means of dilatation of the coronary blood vessels, which is more lasting than that of nitrite. The Zuelzer and the Haberlandt preparations do not exercise these effects which the clinicians have determined to consider as heart hormone.

On the Organ-Specific Growth-Promoting Action of Homoplastic Epithelial Cell Transplantation. — H. G. Zwerg. (*Deut. Zeitschr. Chir.*, **218** : 289, 1929.)

Very often the present homoplastic parathyroid gland transplantation in human beings for combating tetany has been refused and the internal or organ therapy *per os* has been applied as the more active. However, it has been shown that this is not always the case. For, if this were so, naturally nothing.

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ought to come of transplantation. Recently, an organ preparation from out of the cortex of the parathyroid glands has often been introduced into the therapy of tetany, the Collip Parathormone. The experiences here are not unified and are too few in number to permit any extensive criticism on the efficacy. The therapy may be accomplished either by the proper organotherapy, internally, by the administration of parathyroid gland preparations, or surgically, by the transplantation of epithelial cells. Besides the specific organ therapy, a non-specific also was investigated, by means of administration of thyroid gland extracts or thyroid gland transplantation. Only a few observers, however, have reported favorable results on this. On the other hand, many favorable communications concerning the effect of parathyroid tablets have been found. Yet, reports of unsuccessful results are not lacking. An absolutely certain, active method of treatment of human tetany does not exist. As the latest medium, however, the homoplastic transplantation of epithelial cells is offered.

Concerning Coma Diabeticum. — Hermann Bennhold. (*Zentr. inn. Med.*, **50** : 881, 1929.)

By means of insulin which occasions the chief harm in coma diabeticum, other severe injuries to the organism which had remained unobtrusive up to the present, were brought out, above all disturbances of the circulation. Besides camphor preparations as therapeutic measure the author administered adrenalin and likewise tested pituitary and strychnin. With the exception of the passing success with adrenalin, no other particularly certain and effective medium was found.

Secondary Effects of Insulin. — Bonem. (*Münch. med. Wochenschr.*, **76** : 1585, 1929.)

A report on a patient, female, who presented an idiosyncratic reaction to insulin, and the presentation of an analogous case from the literature. Likewise two non-diabetics showed the secondary effect of insulin in the sense of a parenteral irritant substance. The observations warrant the assumption of a substance in the insulin preparation, which causes a secondary effect in the sense of a parenteral or enteral albumin action, and under the circumstances imperils the brilliant effect of the insulin therapy as well.

General Information concerning Hormones. — Leon Asher. (*Fortschrit. Therap.*, **5** : 564, 1929.)

Besides thyroxin, adrenalin, insulin, parathyroidin, and the hormones of the pituitary and the sex organs, in his report the author also treated with the following hormones:

Cortin, the so-called Automatine, the wound hormone, the regeneration hormone, cholin, cholate, etc.

With regard to the question of whether the physiological experiments offer more favorable testimony for the application of pure hormones or other organ preparations, the author comes to the conclusion that the pure hormone preparations are to be preferred. For certain hormones the "all or nothing" law is valid, for others the phase relationship, the reversal to the contrary or the physiological activity. The regulation principle of the humor, presented by the author is of great importance. The disposition of the tissues for the effect of the hormone is either endogenous or exogenous. The influence of other hormones is of first rank among the endogenous factors. To the exogenous factors belong the effects of combinations of nutrition, climate and pathological processes.

The Presence of Female Sex Hormone and Hormone of the Anterior Lobe of the Pituitary in the Blood and Urine of the Newly Born. — R. Brühl. (*Klin. Wochenschr.*, **8** : 1766, 1929.)

From the exhaustive investigations of the author the following results were derived:

1. In the urine of the newly born, without differentiation as to sex, female sex hormone may be demonstrated up to the fourth day. Likewise it is regularly present in blood from the umbilical cord and in liquor amnii. It was not found in the milk in all instances.

2. The hormone of the anterior lobe of the pituitary — Reaction I according to Aschheim and Zondek — could be demonstrated in the urine of the newly born only until the second day and only in half the cases. In the blood from the umbilical cord it is always present, but in various concentrations. In the liquor amnii of older children it was not observed and in the milk only once.

3. In animal experiments it was demonstrated that the occurrence of the secretion of the mammary glands is associated with the

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disappearance of the female sex hormone from the body.

4. Likewise it was shown most evidently in newly born children that the mammary gland secretion is to be associated with the disappearance of the female sex hormone.

Impetigo Herpetiformis in Post-Operative Tetany and Parathyreoprivic Cachexia. — Felix Danisch. (*Frankfurter Zeitschr. Path.*, **38** : 290, 1929.)

In diseases of the glands of internal secretion the relation of the vegetative nervous system has been but slightly investigated up to the present; for only a few endocrine glands, for example the adrenals, the thyroid gland and pancreas is the "closed functional circle" (Asher) of both systems well known. Indeed the author brings out known, but little credited facts: Each alteration in functional condition of an endocrine gland incurs a change in the functional status of the vegetative nervous system. The correlative changes in other endocrine glands in the case of disease of one of the incretion organs is to be explained as partly humoral, *i. e.* by direct incretion effect, partly due to the accommodation of the vegetative nervous system. At any rate the direct or the correlated impairment of the function of one, under the circumstances, seems also to be reflected in the several incretory organs and by means of change in ion concentration and disturbances of calcium metabolism leads to a dysfunction of the vegetative nervous system. In all disorders of calcium metabolism, besides the loss of calcium, the shifting of the blood calcium, ionized and bound to the albumin substance, is very important. Besides epithelial material the thymus, thyroid, pituitary and the sex glands also have an influence on the calcium metabolism. In impetigo herpetiformis in males and likewise in non-gravid women one invariably finds clinical evidences which permit conclusions as to the functional disturbance of the organs mentioned.

Of What Significance Is the Determination of Basal Metabolism for the Practicing Physician. — Fritz Fleischer. (*Zeitschr. ärztl. Fortb.*, **26** : 593, 1929.)

In therapy the calculation of the basal metabolism has shown that in the case of hypofunctioning of the thyroid gland, thyroid gland preparations (thyroxin) can elevate the basal metabolism. In hyperthyrosis antithyroidin Moebius, ovarian preparations, ergotannin and röntgen as well as radium radiations lower the basal metabolism. Hypofunction of the ovary was favorably influenced by sex gland preparations. The substance of the posterior lobe of the pituitary leaves the respiratory quotient uninfluenced, but effects an increase of O_2 and CO_2. The anterior lobe substance of the hypophysis raises the respiratory quotient and offsets the O_2 and CO_2. In blood diseases thyroid gland preparations prove effective.

Concerning the Ovarian Hormone Effect on Several Skin Diseases. — Sergei Borman. (*Dermatol. Wochenschr.*, **89** : 1441, 1929.)

The etiology of a very stubborn eczema such as urticaria univers. is given. Eczema, pruritus and acne vulgaris, under the circumstances were referred to endocrine disturbances in the main. Doczy, for example, applied the Lüttge-Mertz ninhydrin reaction with ovarian extracts as test organ in several of the skin diseases. The reaction gave a positive result forty times in 120 cases of psoriasis. Pariser presented four cases of very severe urticaria which were permanently cured after 6 weeks with ovarian or testicular preparations. Likewise the communication of Pidona and other authors on the association of alopecia areata with menstrual defect give proof of the relation of hormonal activity of the ovary and skin alterations. For further clarifying the problem röntgen therapy has a particular advantage. Especially in Russia where the need for a reliable ovarian hormone preparation has at once been felt, the röntgen experiments have a particular therapeutic interest.

Stomach Function Tests following Liver Therapy in Cases of Pernicious Anemia. — Fritz Brauch. (*Fortschrit. Therap.*, **5** : 412, 1929.)

Isolated contributions have been known concerning the fact that after liver therapy in pernicious anemia the production of HCl is again instituted in the stomach. In five of the cases investigated by the author no formation of HCl occurred after histamin injection, in all cases it was a question of a histamin-resisting achylia despite previous liver therapy. Further researches showed that in no case was pepsin or pepsinogen present.

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From the observations of the author it is shown that in the indicated cases the liver therapy effects no success with reference to an influence on the achylia gastrica.

Concerning the Relation between Joint Disorders and Sex Glands in Women. — W. K. Fränkel. (*Fortschrit. Therap.*, **5** : 513, 1929.)

It is a well known fact that during the premenstruum or the menstrual period, rheumatic processes commonly recur. The most common complaints of patients in business is pain in the joints. Most all of these women with the complaint mentioned are just about to enter the menopause or are experiencing it. No doubt the termination of the mutual internal secretion function can be considered the inciting agent for the chronic knee and joint arthropathy of all these women.

Menge was able to demonstrate that the chronic joint disease had a direct relation to the function of the ovary. He mentioned the disease arthropathia ovaripriva. The institution of a therapy with ovarian preparations, however, first brought disillusionment; nevertheless the failure of the result did not lie in the theoretical premise which led to the test with ovarian therapy, but rather in the inadequacy of the preparation administered. Since new preparations now contain standardized ovarian contents, the great need of the therapy for chronic arthropathy may be fulfilled.

In endogenous obesity and arthropathia Zimmer reached the conclusion that thyroid gland therapy effects extensive improvement in joint diseases, even before obtaining a decrease in weight.

In any case, in the disease mentioned, the question is not only one of ovarian, but also an etiologically important influence on the part of the thyroid gland. The author formerly demonstrated on this matter that the predominance of varices in women and the usual occurrence of varices in pregnancy permits the conclusion of an ovarian endocrine component.

The author derived encouraging results with doses of thyroidin. Joint pains during puberty without infection, are often found in existing hyperthyrosis. Besides ovarian insufficiency and the symptom of hyperthyrosis, participation of the adrenals can also usually be demonstrated. A pluriglandular process is evident in this disease.

A Symptom Complex in a Patient on Insulin Dosage. A Contribution to the Theory of Hypoglycemia. — Yairo Hattori. (*Münch. med. Wochenschr.*, **76** : 1634, 1929.)

As is known, sugar is used with insulin injection to forestall the outbreak of a hypoglycemic symptom complex. However, the author observed almost without exception, in the treatment of diabetic patients, a nervous symptom complex: Lassitude, a feeling of faintness in severe cases, even if there were only a transient comatose condition. When grape sugar was used the symptom complex occurred stronger than with levulose. This indication is dependent upon the amount of insulin injected and can be present without the accompanying hypoglycemia. After repeated injections of the same dose of insulin the symptom gradually fell away and in the end disappeared. One must assume an indication of poisoning and perhaps there is a substance such as, for example, glucosone, in the process of intermediary sugar metabolism. An analogy is to be found in the administration of thyroid gland substance, in which a group of symptoms such as tachycardia, tremor, high blood pressure, etc., can be brought out by thyroglobulin as well as other symptoms of increased metabolism, diuresis, etc., may be brought out by means of thyroxin.

Observations on the Therapy of Senium Praecox. — L. Heumann. (*Fortschrit. Therap.*, **5** : 454, 1929.)

The main condition of senium præcox is hypofunction of the sex glands and of the pituitary lobe. The symptoms of underfunctioning of incretory glands are naturally much less pronounced in the prematurely aged than in hypogenitalism or in castration. In the treatment of senium præcox, to which symptoms alveolar pyorrhea belongs, along with the administration of active incretions, primarily, psychologic agents are standard. Just recently the investigations of Zondek and Aschheim have again revived the discussion of the efficacy of sex gland extracts. The fact is that many of the preparations long known in test experiments according to Allen and Doisy, have shown themselves to be quite inactive. On the other hand, the evidence of Kauder is valuable, namely that single preparations found to be inactive can be made active in combination with other

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active substances. On this basis, disregarding the polyglandular limitations of senium præcox, the relevant treatment was that with a combination of all the glands of internal secretion. The patient received five tablets daily consisting of extracts of testicles or ovary, of placenta, of prostate, of liver, of adrenals, of thyroid and of pituitary and three times weekly an intramuscular injection to supplement the *per os* therapy. The successful result occurred after 3 to 4 weeks. The basal metabolism was raised, the specific dynamic albumin reaction was improved and the spastic atonic symptom complex of Müller was no longer demonstrable. The alveolar pyorrhea is on the decline, potency is increased.

Concerning the Changes in the Organs after the So-Called Regeneration Method. — Kornitzer. (*Med. Klin.*, **25** : 1387, 1929.)

The author maintains, according to his own experimental investigations, that the oral administration of desiccated substance of the testicle is better than the injection of testicular extract.

The opinion that the interstitial cells are the agents of incretory testicular function has been dropped by most authors.

Spleen Therapy in Bone and Joint Diseases. — H. Kuss. (*Med. Welt*, **3** : 1334, 1929.)

A report on the results of spleen therapy in seventeen patients. Daily dose about 100 gm. for 4 weeks, after a pause of about 3 weeks the spleen therapy was resumed. The author has it in mind to make concurrent investigations with spleen extract, but owing to a lack of suitable preparations this is not possible.

In ten of the seventeen patients an effect on the disease process was observed after spleen therapy, but it was not so great as the effect observed with general treatment. In six patients the condition remained practically uninfluenced, in three of these cases, in spite of the spleen treatment, a change for the worse occurred. Blood corpuscle pictures and the depression remained unaltered. In the great majority of cases an increased secretion of pus was observed. After a course of spleen treatment twice during 4 weeks, a definite improvement was seen in only three instances.

The Practical Significance of Hormone Therapy in the Treatment of Women. — Jaschke. (*Fortschrit. Therap.*, **5** : 565, 1929.)

According to clinical experiments the activity of the new sexual hormone preparations doubtless stands fast, and particularly with peroral administration. Failures rest either upon false indication or on insufficient dosage. First, as test for the effect attained is the menstruation-releasing or increasing activity as well as the growth effect; secondly, the regulation of the tempo of the cycle of intervention in cases of oligo- and hypomenorrhea.

Concerning the hormone of the anterior lobe of the pituitary, up to the present, useful mediums for practical application can not as yet be offered. The best results are to be had in secondary amenorrhea or in too seldom or too scanty menstruation of varied origin. A second important field of application is in cases of sterility in hypoplastic uterus. The preliminary results are only slightly satisfactory in primary amenorrhea, following high degrees of hypoplasia of the uterus. Yet, perhaps, in the future, still further success will be obtained with collaboration of the hormone of the anterior lobe. On the other hand, the sexual hormone exhibits pronounced service in climacterium præcox, the symptom of young, operatively castrated women. Striking success was obtained in arthropathia climacterium, however, the author warns against the administrations of preparations without due control.

Experimental Studies on Animals in Parabiosis, with Regard to Physiology and Biology of the Sex Hormone. — E. Fels. (*Arch. Gynäkol.*, **138** : 16, 1929.)

In a parabiosis between male and female the testicle degenerates first; contrarily, the ovary remains unaltered microscopically. In intense degeneration of the testicle castration symptoms are also evident in the pituitary. The assumption of an antagonism of male and female sex hormone is thus justified. On this score the female sex hormone may be considered the stronger biologically. The castrated parabiotic partner was not affected by the sex hormone of the normal animal. The cause of the genital changes in the normal animal in parabiosis with a castrated animal is the hormone of the anterior lobe of the pituitary of the castrated animal. The hormone of the anterior lobe of the pituitary

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passes over to the parabiosis partner more easily than the sex hormone. This observation is hence of practical significance, for in this case smaller doses are required to obtain the absolute effect or possibly, the hormone of the anterior lobe of the pituitary was not secreted so rapidly. Cramps in the non-pregnant parabiotic partner could be observed during the birth process in the companion, so the assumption of a toxin formed in birth must be declined.

In parabiosis between male and female conception and pregnancy only occur after total degeneration of the testicle. An already existing pregnancy was intercepted by means of the antagonism of the sex hormones, as long as a functionally capable testicle is present.

Contribution to the Ferment Theory of Acne and Furunculosis. — Ernst Less. *Arztl. Rundschau*, **39** : 167, June 10, 1929.)

Furunculosis and acne often occur with disturbances of the digestive processes. Among the organs which supply the most important digestive juices is the pancreas. The internal secretions of the pancreas gland have an important effect on carbohydrate metabolism. For supplementing the pancreas ferment in furunculosis, therapy with living yeasts is particularly indicated. In the preparation of Vial and Uhlmann there is a combination of pancreas substance and yeast ferments with which the author obtained good results in the treatment of furunculosis and acne. The preparation shows itself to be a very good adjuvant through its power to greatly elevate the metabolism when used with local treatment with salves and radiotherapy for the treatment of furunculosis and acne.

The Process of Sterilization of Females. — A. Laffont. (*Gynécol. et obstet.*, **20** : 304, 1929.)

Noteworthy advances have been made in late years in the sterilization of animals by means of laboratory methods. It is possible to sterilize a laboratory animal temporarily with a subcutaneous injection of sperm. The sperm injection does not appear to act either on ovulation or on the ovary. It is possible that in this case a sterility is derived by means of sperm toxication of the uterine and vaginal secretions An attempt has been made to sterilize women by sperm injections; positive results appear to have been obtained here, but the process still stands in its infancy and is therefore not ripe for decision. The sterilization tests by means of ovarian extracts or transplants, as well as with placenta and fetal extracts lead to both short and long sterilization. By means of injection of corpus luteum disappearance of the menses and sterilization can be effected. Very interesting results have been reported with reference to this problem in women.

Folliculin acts to inhibit the nidation of the ovum, as has been seen in animal experiments.

Cotte in France and Vogt in Germany have shown with reference to insulin that in duration as well as intensity of menstrual bleeding, normally menstruating women undergo a decrease through the use of insulin. For this reason these authors have administered insulin treatment in menorrhagias of ovarian origin. Apparently the insulin takes effect on the ovarian follicle, thus inhibiting its development.

If the extract of the anterior lobe of the pituitary be injected into laboratory animals a sterilizing effect is derived; administered in weak doses the substance of the anterior lobe of the pituitary induces a rise in ovulation with increased activity of the whole genital tract. Given in large continuous doses the anterior lobe of the pituitary causes a follicular atresia with cystic degeneration.

Diabetes and Acromegaly. — Eric Martin. (*Rev. méd. Suisse Romande*, **49** : 693, 1929.)

Through investigation and study of pituitary extracts it has been possible to differentiate various substances of more or less definite activity; none of these substances, however, can be considered as the product of physiological secretion. On this score, the fact that the most active extract of this portion which is derived from the posterior lobe must be considered as particularly paradoxical. The anterior lobe which has a glandular constitution, supplies only slightly active products which, it seems, regulate the involution of the genital organs. Collin assumes that the so-called posterior lobe extract is the secretion product of the cells of the anterior lobe which accumulates in the intermediate zone and arrives in the region of the infundibulum. Recently it was actually possible for Abel to extract a crystallized substance from the

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posterior lobe as well as from the tuber, which possesses the characteristics of the pituitary extract.

Disturbances of sugar metabolism are usually found in diseases of the pituitary. In diabetes with acromegaly an ample explanation is found either through the hyperglycemic effect of the pituitary hormone or through tumor compression on the nervous centers of the infundibulum. On the other hand it is plausible to assume that these disorders are related through a hyperfunction of the pituitary with coincident alterations in the pancreas. There are cases of diabetes that may be considered as pluriglandular syndromes.

The Vegetative-Hormonal Regulation of the Skin. — Erwin Pulay. (*Wien. klin. Wochenschr.*, **42** : 1212, 1929.)

The significance of liver and spleen therapy for the treatment of skin diseases was extensively discussed and it was shown to what extent the determination of energy metabolism in association with the calculation of blood electrolytes affects the point of attack for treatment of skin diseases. The significance of the hormonal-vegetative system in conjunction with the splanchico-peripheral system was treated exhaustively. Information was given as to the effect of insulin and the experimental researches of Ernst Friedrich Mueller were minutely discussed.

The Sexual Hormone, the Placenta and the Newly Born. — E. Philipp. (*Zentr. Gynäkol.*, **53** : 2385, 1929.)

In the urine of the newly born there is found regularly from the first to the third day, a substance which can effect estrus in the castrated mouse, occasionally, in smaller amounts, up to the sixth day. This substance is found in the fetal ectoderm of human beings. Likewise, one can find in the urine of the newly born a substance which can induce the same changes in the ovary of an infantile mouse as does implantation of anterior lobe of the pituitary. This substance is identical with the hormone of the anterior lobe of the pituitary of the mother. The accuracy of the pregnancy reaction of Zondek and Aschheim, which is based on the excretion of this substance in the urine of the pregnant women, is confirmed. In the urine of a child a substance can be demonstrated which acts on the ovary of infantile mice by effecting ripening of the follicles and permits the consideration of an activity of the anterior lobe of the pituitary in the growing organism. The researches of the author extensively confirm the existing views on the basis of clinical observations, concerning the function of the placenta.

The Changes in the Endocrine Glands in Lead Poisoning. — Peisaschowitz. (*Virchows Arch. path. Anat. u. Physiol.*, **273** : 276, 1929.)

The lead accumulating in the blood induces atrophy of the thyroid gland, a weakened activity of the chromaffin system, an accretion of fatty substance in the adrenals and a diminution of formation of semen. The morphological changes which proceed in the incretory organs under the influence of lead poisoning, confirm the existence of a disturbance of the incretory equilibrium in the endocrine gland system.

Researches with Peroral Insulin in Diabetes Mellitus in Children. — M. Ottow. (*Münch. med. Wochenschr.*, **76** : 1584, 1929.)

In two young diabetics (14 and 15 years old) with 18 or 50 to 90 gm. of sugar in the urine daily, insulin preparations were given *per os* by Dr. Stephan and their effect observed. The result was slower than that with subcutaneous application. The disappearance of sugar from the urine precedes the decrease in blood sugar at one time. The preparation causes no harmful secondary effects. With gastrointestinal administration there seems to be an accumulation which effects an increased tolerance by means of further generation in the island apparatus.

Clinical Investigations on the Effect of Intravenous Insulin Injections. I. Blood Sugar Curves in Normal Individuals. — A. Norgaard and Th. E. Hess Thaysen. (*Hospitalstidende*, **72** : 881, 1929.)

The author applied the process of calculating the glucose metabolism under insulin effect which has the advantage of giving a direct index for the glucose amounts which the organism can metabolize under the influence of insulin as this potentializes the "degree of assimilation" or the "degree of tolerance." With the aid of this method one

(*Continued on page 298*)

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can determine how much blood glucose in per cent, calculated per minute, can be oxidized after an intravenous injection of 12 insulin units. In nine men and nine women a typical curve was found after 12 insulin units. The first portion of the curve exhibited a decrease of blood sugar values, after the depression there followed a rise in values. These two portions of the curve the author indicated respectively as 1. "Transformation curve" which indicates the amount of glucose in the blood which is transformed under the insulin effect in the organism, and 2, the "Construction curve." The metabolism figures show in per cent the amount of glucose which was transformed in a minute from the blood glucose present before the injection.

The Adrenalin Content of the Blood in Narcosis. — H. Schlossmann and H. Mügge. (*Arch. exp. Path. u. Pharmakol.*, **144** : 133, 1929.)

The authors investigated the question of whether, during narcosis, the content of adrenalin in the blood stream is increased, and that by means of this the adrenalin impoverization of the adrenals is explained. The following was observed:

In the peripheral blood adrenalin is always first demonstrable when the blood pressure begins to fall. None of the narcotics investigated induced an exhaustion of adrenalin. The adrenalin exhaustion is rather an indirect effect of the narcosis and the result of decreased blood pressure. Following the termination of the narcosis the adrenalin exhaustion continues for a long time, even though the blood pressure promptly rises again. Under normal conditions adrenalin is not required to maintain blood vessel tonus, but immediately becomes vital when the normal regulation fails. Information has previously been presented by Delbet and Ogawa concerning the clinical significance of the impoverization of the adrenals directly by means of chloroform narcosis. Evidently by means of chloroform the new formation of adrenalin in the adrenals is inhibited.

Clinic and Therapy of the So-Called Hemorrhages of Puberty. — Runge. (*Med. Welt*, **3** : 1394, 1929.)

The author made therapeutic investigations with ovarian preparations but observed no success in his cases. This lack of success is due to the fact that the presence of this

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hormone in metropathia hemorrhagica is considerably higher in degree than normally. A hormone influence on this disease can only be accomplished if it is practically possible to derive the second ovarian hormone namely the secretion of the pregravid, transformation-effecting hormone of the corpus luteum.

Concerning the Hypophysin Therapy of Kidney and Ureter Calculi. (With Several Observations on the Motility of the Human Ureter.) — W. Schöndube. (*Zeitschr. Urol.*, **23** : 865, 1929.)

The reports of the few authors who have been occupied with the investigation of hypophysin therapy of calculi in the ureter as presented by H. Kalk, are not very encouraging. According to the author's investigations, despite the insignificant results of other authors, hypophysin seems to maintain its place in internal therapy as a supplementary medium. In 21 individual cases treated with hypophysin the author observed elimination of one or more concretions ten times, in one case three times within the course of a year. Hence in about 50 per cent of 21 cases a successful elimination of the calculus was obtained after hypophysin treatment, concerning which it may be said with reservations, that the therapy is usually to be combined with glycerin lemonade, several hours after the hypophysin injection, often also with ureter catheterization and water douches. In all criticism concerning post hoc propter hoc, it must be assumed, however, that in a portion of the cases mentioned the effectiveness of hypophysin injection in elimination of the calculus can not be gainsaid. In many cases, certainly, one derives the impression that hypophysin was quite ineffective, in spite of the fact that it had not been given in vain. The author thinks that the hypophysin by means of which he was able to observe increased ureter peristalsis cystoscopically, gradually disengages the calculus so that a douche is capable of dislodging the concretion. The result is that in many cases a very refractory calculus causes severe colic or pains after hypophysin, while a stone lying in the distal portion of the ureter, even with rather intense hypophysin peristalsis, seldom causes colic. In severe septic disease symptoms the author bars the use of hypophysin treatment. Hypophysin is no medium for promoting spasms, but rather a substance which enhances the normal course of the peristaltic process, in contrast to pilocarpin (Katsch). In kidney calculi the indication for hypophysin therapy is less favorable than in cases of ureter calculi.

Several Investigations into the Effects of Thyroid Gland Preparations. — Shimazono. (*Klin. Wochenschr.*, **8** : 1789, 1929.)

The injection of thyroxin into the lymph system in rabbits, in one-tenth the dose, acts on basal metabolism one hundred times as strong as the intravenous dose. The action is not altered by severing the cervical sympathetic. On the other hand, injection of thyroxin into the lymph has no effect on the water metabolism. A direct influence on the metabolic center was assumed, which is certainly evident since the tissue respiration of isolated tissue is not changed by thyroxin. Also hypophysin acts in the lymph much more strongly than in intravenous application. In suitable dosage thyroid gland preparations promote the regeneration of peripheral nerves, which was proved experimentally on the ischium and therapeutically in polyneuritis.

Contribution on the Calculation of Quantities of Sexual Hormone. — Siebke. (*Zentr. Gynäkol.*, **53** : 2450, 1929.)

The presentation of a scientific, objection-free and successful hormone therapy is the knowledge of the hormone quantities with which the body normally functions. In addition, it is important to know directly in which diseases there is a lack and which an excess of hormone. During the menstrual cycle the hormone concentration in the blood reaches its height on the 3rd day before menstruation. Hence, therapeutic doses of hormone as supplement give the best results from the 12th to the 3rd day before the expected menses, or the 17th to the 26th day of the 28 day cycle.

In the circulating blood of the normal woman during the menstrual cycle there is found from less than 100 mouse units to more than 200 mouse units of hormone. During pregnancy the hormone concentration in the blood rises higher than during the cycle. The determination of hormone in the blood of amenorrhea subjects confirms the fact that there are fluctuating cycles. According to the results of the author indication is given of the height of the fluctuating curves of hormone therapy. In cases of metropathia

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hæmorrhagica the sex hormone content of the blood may be increased in the period between and hence the therapy with sexual hormone is unsuitable. During the first week of the metropathic hemorrhage the hormone concentration in the blood is raised, hence a therapy with sexual hormone is not applicable.

Internal Secretion and Psychic Processes. I. Hormone Reflexology. — W. N. Speranski. (*Abhandl. a. d. Neurol. Psychiat. u. ihren Grenzgeb., Monograph,* No. 52 : 1, 1929.)

The "emotiogenic" (em.) hormone is in the main the derivative of the hormone. There is every reason to assume that, for example, the "disquiet-emotion" is linked with the activity of the thyroid gland. After continued mental excitement associated with a feeling of anxiety an important increase in the size of the thyroid gland may be observed. Imbecilic quiet has been observed in myxedema.

The hormone of the sex glands has a general stimulating effect on the organism and possesses no emotional properties. However, under certain other influences an excessive reflex decomposition of this hormone may occur which induces an erotic emotion.

Cannon reported on an increased amount of adrenalin in the blood of infuriated cats. Adrenalin itself possesses no "emotiogenic" property. The manifestations of cyclothymia, the maniacal depressive psychosis are associated with cyclic disturbances of the equilibrium in the system of hormone formation. If hysteria is dependent upon an underdevelopment of a portion of the nervous-psychic apparatus, associated with the underdevelopment of several hormone-forming organs and coordinations in the system of hormone formation, then the catatonia of puberty may be explained as a premature development of a portion of the nervous-psychic apparatus (including the hormone producers).

Concerning the Peroral Action of Insulin and Peroral Insulin Therapy. — Richard Stephan. (*Münch. med. Wochenschr.*, **76** : 1579, 1929.)

The author conducted very extensive researches on the peroral administration of insulin. For administration in mechanically suitable dispersion preparation dry insulin or insulin salt, suspended in a digestible fat or oil colloidal and in various admixtures, was given on an empty stomach. It was thus demonstrated that with peroral administration, the essential condition for resorbability is fulfilled in prompt release of the bile reflex and in intrastomachal presence of an insulin-bile acid relationship. The bile-acidic insulin requires no protection, it is not destroyed in the fasting stomach. In experiments with diabetics it was shown that the true insulin effect occurs after the ingestion of food. Peroral insulin administration discloses a rather important deposition effect in the organism which, as opposed to all experiments thus far, is to be considered novel, in other words, that in the fasting period total insulin effect is in no wise obtainable.

For the individual case there exists an optimal peroral dose which has the maximum effect on the blood sugar curve.

The results of the author permit the affirmation of the value of peroral insulin therapy.

Internal Secretion and Internal Medicine. — W. H. Veil. (*Fortschrit. Therap.*, **5** : 564, 1929.)

The hormone has been developed into a very favorable adjuvant remedy. In handling it the practicing physician must consider that the hormones are related to definite organs which give rise to them, that they do not merely serve as substitute preparations for these organs or the lack of their function. Only in a small number of cases must substitution be made with hormones. The classical examples in this instance are the substitution of thyroid gland function and of liver function in pernicious anemia. On the contrary, insulin is not precisely a therapy for diabetes.

The hormone can be employed for therapeutic effect quite dissociatedly from the fundamental activity of the internal secretory gland, thus the hormone of the thyroid gland can be used in treatment of emaciation, etc. The interrelation of hormone therapy and plant poison therapy is important. Adrenalin, for example, by relieving the unfavorable influence of digitalis on the respiratory organs, can produce a favorable result in digitalis therapy. Likewise, adrenalin can relieve kidney contraction due to the action of digitalis. In the heart itself adrenalin can aggravate the transfusion from auricle to ventricle and even inhibit it (heart block). Thyroxin is capable of dispersing this unfavorable effect.

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Hormone therapy must also be administered with very careful observance of the unit content. The author reports that in one case of pernicious anemia the condition was brought to one of sugar disease by means of the administration of raw liver. This unsatisfactory result was explained thusly: that in raw liver there is present another hormone besides the one with favorable influence on pernicious anemia, namely the glycemin discovered by Loewe. The occurrence of the sugar disease in this case is to be ascribed to the action of the glycemin.

Is It Possible to Influence the Internal Secretion of the Pancreas Operatively? — R. Demel and E. Krammer. (*Mitt. Grenzgeb. Med. u. Chir.*, **41** : 582, 1929.)

On the basis of animal experiments the authors come to the conclusion that the internal secretion of the pancreas is not to be influenced operatively, at least as far as is known by present methods. There is hence no claim, provisionally, to apply this process to human beings.

Hemorrhages during the Change Years. — B. Wolff. (*Zeitschr. ärztl. Fortb.*, **26** : 591, 1929.)

Occasionally good results were obtained with pituitary preparations of various kinds. In addition, ovarian preparations and a local therapy with dabbing of the cervix with adrenalin was instituted.

Experimental Investigations on the Physiology of the Genital Tract in Females. — Rudolf Dyroff. (*Arch. Gynäkol.*, **138** : 362, 1929.)

From the corpus luteum or the ovary all sorts of chemical derivatives have been obtained which actually cause the formation of more or less artificial decomposition products, which must not be placed on the same basis as the true internal secretion because they are capable of exercising a more or less specific biological function. This likewise holds true for the new ovarian preparations of Zondek and E. Laquer, though with these, in amenorrhea cases, normal menstrual processes were initiated more often than previously with similar extracts and although the author himself was able to induce a uniformly increased genital plasia with these in rabbits. At any rate the Zondek preparation evidently contains the hormone of the corpus luteum in higher concentration than formerly, however, one must not exhibit this as an estrous hormone, for estrus, and also ovulation, was not induced, but rather a hyperemic process in the genitals.

Knowledge concerning the histological-chemical similarity between corpus luteum and adrenal cortex has long been obvious. (Mulon and Wallart.) Mulon goes so far as to say that the corpus luteum is a temporary adrenal cortex. However, indications accumulate that one has to look for the physiological counterpart of adrenalin for the tonus of the parasympathetic in the body in the secretion of the adrenal cortex. Cholin is to be regarded as the physiologic parasympathicotonic for the intestine. As proof of the possibility of a similar internal secretory effect of corpus luteum and adrenal cortex, the fact may be presented, too, that pubertas præcox occurs with tumor of the cortex of the adrenals. As an outcome of this the whole strikingly fine development of the female genitals in the newly born (excessively large adrenals) is comprehensible. Whether the disputed internal secretion of the corpus luteum belongs to the cholin group is undecided. However, we have here a secretion which has specific parasympathicotonic properties.

Hypophyseal Diseases. — F. Boenheim. (*Zeitschr. ärztl. Fortb.*, **26** : 617, 1929.)

The hormone of the pituitary exercises an extensive influence on the collective organs of the human body. Very often disturbances of growth attend diseases of the pituitary. In pituitary dwarfism the therapy is generally little effective. Falta recommends the injection of extract of the anterior lobe in the so-called third growth period, *i. e.* after the 13th year of life. For genital dystrophy this medication is almost always invalid for human beings. In dystrophia adiposogenitalis pituitary preparations have been given repeatedly, particularly in combination with thyroid gland. Though Falta states that only severe dietetic cases are to be influenced, this does not coincide with the author's opinion. The importance of the pituitary for the circulation is definitely determined. The pituitary hormone presents a factor for the regulation of blood pressure. By injections of preparations of posterior pituitary it is possible to increase the blood pressure. Further, the possibility

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of inducing contractions of the gall bladder by means of pituitary preparations is therapeutically important. The same holds true for the intestines, so that striking results may be obtained in many spastic forms of obstipation. The influence of pituitary preparations on diuresis in healthy and diseased individuals is not effective with peroral dosage, but is efficacious in injection and in rectal administration in the form of suppositories, of which fact the author was convinced by a whole series of tests.

The Gottlieb School relates paradentitis to disturbances of the pituitary (Weinwann) which, however, occurred in only one-fourth to one-fifth the author's cases.

Relation between Age and Thyroxin Activity. — E. Abderhalden and E. Wertheimer. (*Zeitschr. ges. exp. Med.*, **68** : 1, 1929.)

From the investigations of the authors it is shown that the activity of thyroxin, measured with regard to body weight and age, is in close relation with the age of the animal. With increasing age the thyroxin effect, in the relation mentioned advances more and more. The loss of glycogen is accomplished more slowly in growing animals than in adults. Young and adult animals, in general, lose fat in the same degree; likewise with regard to gas metabolism and nitrogen metabolism no difference was observed in both young and old animals with respect to thyroxin effect.

Concerning the Female Sex Hormone, Menformon, Particularly Its Antimasculine Effect. — E. Borchardt, E. Dingemanse, S. E. de Jongh and E. Laqueur. (*Zeitschr. ges. exp. Med.*, **68** : 86, 1929.)

By means of menformon the primary and secondary sex characteristics, in development as well as formation, are influenced in a negative sense. The inhibition is transient and after termination of the treatment is capable of totally disappearing. The antimasculine influence is particularly demonstrated in rats, guinea pigs and rabbits. In young animals about 1 mouse unit per day suffices to institute inhibition after 5 weeks. The "all or nothing" law does not hold with regard to menformon activity, on the contrary the question of dosage is of greatest importance for the strength of the effect. Steinach's evidence that the occurrence of an inhibition of the secondary male sex characteristics in the presence of the testicle with normal formation of semen only signifies that the antimasculine effect immediately seizes upon the genitals themselves, does not seem to the author to be established. The influence of menformon on the male sex organs is specific, for it is not to be observed in any other organs. Mammary and adrenals are augmented. The investigations of the author testify that the inhibiting effect passes over to the testicle.

Concerning the Significance of the Spleen and of the Radial Cell System (Reticulo-Endothelium) for the Prophylaxis of Malignant Inoculation Tumor in the Rat. — B. E. Brüda and H. Pfeiffer. (*Zeitschr. ges. exp. Med.*, **68** : 116, 1929.)

The spleen as well as the rest of the radial cell system (reticulo-endothelium) contributes to the true endocrine glands. In the investigations on rats, part singly and part in parabiosis arrangement, it was shown that the spleen effects a prophylaxis and inhibition of the progress of malignant mouse tumor in the rat. Since this prophylaxis, as has further been shown, is to be considered as the display of a chemically active inhibiting substance, as an internal secretory process, thus the reticulum of the spleen belongs to the endocrine glands.

Concerning Resistance to Thyroxin. — W. Falta. (*Endokrinologie*, **5** : 62, 1929.)

In treatment with thyroid gland tablets it is possible to observe that the effect on individual test persons is often quite varied. The author made observations on a case with symptoms of the central nervous system, which gave definite evidence for the diagnosis of polioencephalomyelitis; this case appeared fairly refractory to large doses of thyroxin or thyropurin. A rise in pulse frequency occurred, but the basal metabolism was not at all changed. The author also observed a second case of resistance to thyroxin, a case of status postencephaliticus. There are animal experiments concerning this, which demonstrate a relation between the resistance to thyroxin and the nervous system. Clinic and experiment demonstrate the possibility that in highly differentiated organisms the metabolism-increasing effect of thyroxin is suppressed according to the conditions of the central nervous system.

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On the Treatment of Psoriasis with Products of Digestion of the Cutaneous Scale. — Vojislav Mihajlovic. (*Wien. klin. Wochenschr.*, **42** : 1192, 1929.)

In the rather inadequate knowledge we have so far concerning the etiology of psoriasis, one must not be surprised that the therapy of this disease is not yet placed on a firm basis and that the physician is thus left to a manifold therapy, in which, not infrequently, he has the sad experience of observing that in very severe cases the disease resists all sorts of variously recommended and applied therapeutic remedies. Such a severe case of the disease gave the author the idea to study a treatment with extracts derived from the skin scale, similar to that which Strümpke (1921) and Vercellino (1924) have done. The author then proceeded immediately in collaboration with Professor Joannovíc in the Institute for General Pathology and Pathological Anatomy, to the application of one of his methods of digestion of scale with pepsin and trypsin by means of the extracts produced by Dr. Tichomirow.

On the basis of 15 months of experimentation in the treatment of psoriasis with digestive products of psoriasis skin scale, according to the method derived by Joannovíc, the author states as follows:

"1. The subcutaneous injection of this preparation brings forth neither local nor general reaction.

"2. At the beginning of treatment an intense skin irritation occurs, while the efflorescence begins to scale slightly and abruptly.

"3. In the process of treatment no characteristic punctiform hemorrhage occurs with removal of the efflorescence and with cessation of the irritating skin symptoms.

"4. The flexing of the joints, painfully hindered by the skin changes, returns again to normal with cessation of the pain.

"5. The leukodermia occurring on the site of the efflorescence, is coincident in form with the efflorescence and is to be differentiated from a leukodermia following chrysarobin. Though leukodermia psoriaticum is extraordinarily seldom, it belongs as a rule to this sort of treatment.

"6. The efflorescence usually disappears first from the scalp, then from the skin of the breast and the abdomen. The changes in the knees and elbows are most resistant as is also the case with other methods of treatment.

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"7. The injections are given subcutaneously, daily or every second, third, fourth or fifth day, in amounts of 1.0 to 5.0 to 10 cc. and are tolerated entirely without reaction. The digestive product given need not originate with the patient himself, but may be successful even if derived from the skin scale of other patients; however, the autologous extracts seem to be the more effective.

"8. This method of treatment, above all others up to the present time restricts the occurrence of relapses."

The results obtained up to the present with this method of treatment, warrant considerable attention and further trial in order, if possible, to obtain still better and more lasting results with it.

The Treatment of Rheumatic Diseases. — A. Zimmer. (*Fortschrit. Therap.*, **5** : 545, 1929.)

Ovarian, thyroid and pituitary are preeminently the glands the disturbances of which can definitely be associated with the cause of rheumatic diseases. Obesity is closely allied therewith. Hormonal therapy in disturbances of internal secretion is not to be regarded as a substitution therapy, but as a causal treatment, for it has been shown that there is involved here not a substitution alone, but a definite length of treatment in order to obtain a restoration of the equilibrium of the internal secretion function.

The Significance of the Thyroid Gland for the Pathogenesis and Clinic of Basedow's Disease. — Georg Büttner. (*Brun's Beitr. klin. Chir.*, **147** : 623, 1929.)

Asher concludes from the varied activity of the thyroid gland secretion that the thyroid gland hormone is the activator of the vegetative automatism. Asher conceives the division of work between adrenalin and thyroxin in such a manner that the thyroid gland secretion is effective as activator in the same places where adrenalin is a stimulant toxin. The adrenalin effect is a rapid, progressive nerve stimulation, thyroxin effect begins slowly and ends slowly. It is not yet known how the combined action of adrenalin and thyroxin takes place. The strongest argument against the thyroid gland theory of morbus basedowi is the impossibility of creating a total Basedow condition experimentally. The acute feeding tests, even with large doses of thyroid are to be considered invalid, the chronic lengthy feeding experiments are not uniform.

If one administers thyroid gland substance in the presence of thyroid gland, to induce an experimental hyperthyroidism, substitution occurs as in myxedema, the incretion substance introduced is not a simple addition, but rather occasions an altered milieu in the organism, which is also supported by the thyroid gland passively.

Arterial Hypertension with the Symptom Complex of the Left Heart. Treatment by Means of a Pancreas Extract. Improvement. — H. Chabanier and P. Truchot. (*J. Urol.* (*French*), **28** : 405, 1929.)

In a 50 year old female patient with hypertension and intense insufficiency of the left heart an unequivocal improvement of the condition was obtained by means of a treatment which consisted exclusively of the administration of pancreas extract. The functional as well as anatomical symptoms which were dependent upon a dilatation of the left heart, showed a very prompt and significant decrease, though the hypertension only first exhibited a retrogression about 6 weeks after commencement of the treatment. It must also be pointed out that the treatment may be sustained without the appearance of any secondary symptoms whatever. On the other hand, report was made previously of the therapeutic effect of various pancreas extracts, some insulin and some other extracts, in hypertension with symptoms of insufficiency of the left heart.

Ovarian Insufficiency with Oligo- and Hypomenorrhea. Pregnancy after Treatment with Extract of the Anterior Lobe of the Pituitary. Disappearance of the Symptoms of Ovarian Insufficiency. — G. Cotte. (*Bull. Soc. obstét. et gynécol.*, No. 8 : 559, 1929.)

A 20 year old female patient came to the author in September, 1927, for treatment. The patient was menstruating scantily, was very fat and showed unquestionable symptoms of endocrine disturbance. Menstruation was irregular, seldom and very painful. The attempt with transplantation of ovarian substance failed, because the transplant was ejected. Finally a test was made with injection of extract of the anterior lobe of the pituitary. In the month following the patient spontaneously reported that she felt much

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better and that she had become pregnant. Since the commencement of pregnancy (4 months) the findings are very good. Without desiring to draw too extensive conclusions from these results, the author thinks that the administration of substance from the anterior lobe of the pituitary deserves consideration. Since the appearance of the publication of Zondek and Aschheim it is known that the anterior lobe exerts a specific and also a stimulating influence on the genital apparatus. It is possible, in animals, by means of injection throughout one day to obtain hypertrophy of the genital tract. The observation of the relation of the follicle of the corpus luteum after injection of the anterior lobe of the pituitary also gives the author the opportunity to treat cases of amenorrhea with injectible extracts of the anterior lobe of the pituitary. At any rate, in cases in which ovulation is lengthy, sluggish or insufficient, the method of administration of anterior lobe extract is to be preferred to that of other substances of endocrine gland origin.

The Nervous Disorders of Biermer's Anemia, and Liver Therapy. — H. Curschmann. (*Münch. med. Wochenschr.*, **76** : 1863, 1929.)

Since the initiation of liver therapy no improvement was seen in the spinal syndrome in pernicious anemia. The effect of liver therapy on the nervous disorders is totally negative. There was neither improvement of the objective symptoms nor of the subjective disturbances, more often there was an increase in the spinal symptoms. Liver therapy failed totally as far as concerned the nervous disturbances.

Hyperthyroidized Animals and Their Progeny. — G. Döderlein. (*Zentr. Gynäkol.*, 53 : 2594, 1929.)

Different authors in recent times propose the administration of incretory organ preparations (insulin, thyroidin) in diseases of metabolism in pregnancy (Dyroff, Gessner, Kermauner, Klaften, Kraul have published such work). Up to the present only very carefully allotted doses have been given, for a short time only, and only at the termination of pregnancy, in order that the symptoms of the actual disease in the mother could be sufficiently influenced without harming the fetus any more. The endocrine therapy may be administered in large doses harmlessly, if a transfer of the substituting hormone to the fetus, and thereby the possibility of harming the fetus, is not to be feared.

This question may be tested in warm-blooded animals. The warm-blooded animals are not to be compared, in their bodily functions, with human beings, but conclusions from animal experiments are permissible. Döderlein has found that in experimental hyperthyroidism the hyperthyroid condition, brought about by a large dose of thyroidin, suppresses propagation in very fertile animals. In the second generation there is remarkable sterility in male offspring of hyperthyroidized animals.

Endocrine therapy is a totally different method of treatment. On this account one must be cautious with application of this therapy in pregnancy, where the fetus also may be affected.

Concerning the Effect of Thyroxin on the Iodin Content of the Blood in Myxedema Patients. — B. Eisler and A. Schittenhelm. (*Zeitschr. ges. exp. Med.*, **68** : 487, 1929.)

The iodin content of the blood in myxedema is very much decreased. Thyroxin is effective in increasing the iodin content of the blood and the basal metabolism. The iodin content of the blood rises to values above normal as soon as the thyroxin effect sets in and in spite of continued thyroxin dosage falls to roughly normal values. There is no parallel between basal metabolism and iodin content of the blood in myxedema patients during the administration of thyroxin. The iodin concentration of the blood of normal persons is not increased after prolonged application of thyroxin.

Report on the Principles of the Male Hormones. — O. O. Fellner. (*Endokrinologie*, **5** : 66, 1929.)

There are at least two male hormones; one male hormone, the counterpart of the female, is the substance which brings about the eventual formation of the male sex characters; its seat is evidently the testicle. The second hormone brings the testicle to maturity and maintains the mature state. Similar to Smith and other contributors the author observed hypertrophy of the interstitial cells, augmentation of the seminal vesicles and growth of the penis following

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injection of the hormone of the anterior lobe. Even with very large doses, injected over a long period of time, the author could not derive maturation of the testicle. According to the experiments of Biedl and Aschner it must be assumed that in the pituitary, in the anterior, intermediary or posterior portion, a hormone was produced which is the impulsive force for the male sex hormone. But this is certainly not identical with the anterior lobe hormone. From his own experiments the author concludes that the gonads are hermaphroditic in regard to secretion, that unquestionably there must be two hormones. The author presents observations on a male whose breasts were fully developed as those of a woman.

The author was able to demonstrate without difficulty that the interstitial cells of the normal ovary produce the female sex hormone. Whether the female hormone derived by the author from the testicle is from the interstitial cells is not yet accorded, however, Fellner holds it as evident. Pseudohermaphroditism and sex modifications therefore, seem to be based upon the fact that between the gonads and the superseding organ there exists a dysfunction.

Corpus Luteum and Sexual Hormone. — L. Fraenkel and E. Fels. (*Zeitschr. ges. exp. Med.*, **68** : 172, 1929.)

The hormone which releases estrus in the castrated mouse is evidently not the female sex hormone. Doubtless it is an important constituent of the female sex hormone. It is the follicular hormone and is also found in the corpus luteum. Moreover, in corpus luteum there is another hormone component which can not be demonstrated by means of test objects and which is not yet presented in manufactured form.

One gains an insight into the question of identity of sexual hormone and corpus luteum incretion from experiments in the clinic. One must firmly grasp the fact that a valuable hormone which contains all the physiological potentialities must also lead to successful therapy as in the case of insulin, thyroidin and adrenalin. It is another matter with the sex hormone preparations. There is no doubt that they are effective in test animals; on the other hand the clinical results, viewed favorably, are to be considered at most mediocre. They are practically null in the case of sterility. The end result and termination of each hormone therapy is the pregravid construction of the mucous membrane of the uterus and the forced menstruation following therefrom. L. Fraenkel in 1927 mentioned 30 per cent results on this score, at best, and he expected an increase in the number of successful outcomes, but the expectation was not fulfilled. The results are very bad in the case of primary amenorrhea, as v. Jaschke has recently emphasized. However, very good results have been obtained with corpus luteum preparations in insufficiency symptoms and sometimes also even in cases of amenorrhea. It will be the task of the future to seize upon all the hormone components and to apply them therapeutically.

Parabiosis and Anterior Lobe of the Pituitary. — H. Kallas. (*Pflügers Arch. ges. Physiol.*, **223** : 232, 1929.)

From parabiosis experiments it is shown that the infantile pituitary produces hormone of the anterior lobe and is capable of giving it off into the blood, and further, that the ovary influences the endocrine activity of the anterior lobe of the pituitary.

Menstruation and the Hormones of Ovary and Anterior Pituitary

(*Continued from page 271*)

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Concerning the Hormone of Heart Action. 13th Contribution. — L. Haberlandt. (*Zeitschr. ges. exp. Med.*, 68 : 185, 1929.)

The author investigated further concerning the heart hormone preparation and determined the super-limits of activity for adrenalin- and histamin-free heart hormone preparations in dilution of 1:100 millions to 1:1000 millions (in 0.5 cc. liquid). With these concentrations on a suitable sensitive heart, the pulse-inciting and pulse-accelerating effects of normal heart stimulation subsistance could be demonstrated. By means of lengthy application of the heart hormone preparation, according to conditions, the excitability of the frog ventricle is abbreviated.

Concerning New Substances with Insulin-Like Effects. (Biguanidin and Its Derivative.) — E. Hesse. (*Münch. med. Wochenschr.*, 76 : 1697, 1929.)

In biological relationship biguanidins have many characteristics in common with synthalin-like substances—polymethylen-diguanidin, as the symptom of blood pressure decrease, hypoglycemic cramps, the palliation of these with grape sugar and the impossibility of alleviating the cramps with adrenalin. Regarding glycogen synthesis in normal animals as well as those deprived of the pancreas, this experiences no difference. On the contrary the effect of insulin on glycogen synthesis is basically different, for with insulin the relief of the insulin cramp with adrenalin, the life-saving effect of grape sugar and above all the characteristic trophic influence of insulin on the dog without pancreas, by which the animal is kept bright, lively and healthy, is evident. All these things are unattainable with biguanidins. This fact is of great importance in the therapeutic application of these substances on human beings.

The Functional Relation between Pituitary and Pancreas. — B. A. Houssay. (*Endokrinologie*, 5 : 103, 1929.)

There are two groups of definite and important facts, namely, on the one hand the functional antagonism between extract of the anterior and posterior pituitary lobes and insulin and on the other hand, the great sensitivity of hypophysoprivic animals to the hypoglycemic and toxic effect of insulin which may be inhibited by means of injection of pituitary extract. Burn noticed that with pituitary extract the glycemia inhibited by the effect of insulin receives a new impetus and the hypoglycemic symptoms can be made to disappear. The extract of the anterior lobe of the pituitary does not have the antagonistic effect of pituitrin. The effect of the posterior lobe extract is specific. Bollinger and Hartmann confirm the experiences of Winter and Smith, that insulin offsets the organic blood phosphorus and the extract of the posterior lobe increases it. Progressive doses of insulin restrict the oliguric action and the hydremia induced by a later injection of posterior lobe extract in laboratory animals and in human beings with water diuresis. According to Pogany and Pinter-Kövats, the injection of insulin before that of posterior pituitary incretion lessens or restricts the arterial blood pressure-increasing effect of the posterior lobe extract. According to La Barre the injection of pituitary extract augments the secretion of insulin.

The Influence of the Anterior Lobe of the Pituitary on the Genital Tract in the Guinea Pig. — J. Watrin. (*Bull. Soc. obstét. et gynécol.*, No. 8 : 574, 1929.)

On the basis of implantation tests on guinea pigs the author was able to derive the following results:

The genital reaction on the part of the pituitary hormone is of a quantitative and not of a qualitative nature. Large amounts of hormone effect very great changes. The uterine reaction is identical with the ovarian or is exactly dependent upon it. The observations of the author are a confirmation of the experiences of Courrier and Kehl, who by another method, namely by injection of increasing doses of pituitary extract obtained alterations which are proportional to the size of the dose.

Gregor Johann Mendel

(*Continued from page 279*)

altercations with political personalities. A final conflict with the German Liberalist Party, especially concerning the property of the religious institution, which he fired with numerous protests, culminated the difficulties of this defiant, liberal-minded abbot, and there began to be surreptitious remarks concerning

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the sanity of his mind. Life became increasingly uncomfortable, with only his nephews and close relatives to cheer him, for they knew and appreciated his idiosyncrasies. On January 6, 1884, rather suddenly, Mendel died of organic heart trouble with complications.

Mendel's place in the scientific world is very definite. Besides being a careful research worker he was a profound thinker. His manner of living particularly suited the work he chose, for the well regulated, easy-flowing life of the monastery offered an excellent setting for the long and tedious experiments which formed the basis for his system of heredity. His contributions to the literature are few: specifically, "Experiments on Plant Hybrids," first published in 1865, and "Meteorological Observations." Letters (published in 1905) to his friend Carl W. v. Nägeli the botanist (written during the years 1866 to 1873) give evidence of the trend of the work on heredity, to which Nägeli often lent inspiration and guidance.

One can not describe Mendel's work on heredity briefly. Fundamentally, however, the work was done on the common pea. His method, unlike other students of this problem, was to trace a single pair of alternative characteristics at one time. He crossed a tall and a dwarf plant and carefully followed the appearance of these two factors alone. The same method was applied to other plants, and likewise, though not so detailed, to animals. He chronicled the results of these experiments. From these excellent researches biologists have been able to extend the application of the principles to unnumbered problems, and thus there has come into the annals of science a "New conception of the nature of living things — and of their potentialities and their limitations." Great economic value has been derived from Mendel's work, also, for it is evident that the breeder of plants or animals is enabled to obtain definite and excellent results if he follows the fundamentals discovered by Mendel.

Unlike the work of Darwin who received immediate recognition from the scientists of the period, Mendel's almost disappeared, for exceedingly little was known of it until 1900, when it was rediscovered by deVries, Correns and Tschermak; but with the resurrection of his work such prompt and extensive advances were made as a result of the knowledge he gathered, that Mendel's fame is now no less than Darwin's.

Liver Diet and Reticulocyte Reaction in Simple Anemia. — J. Wahlberg. (*Acta. med. Scand.*, **72** : 143, 1929.)

The author reports on the clinical investigations regarding blood regeneration in simple anemia under liver diet, as compared with the erythropoietic reaction of iron and arsenic therapy and hospital treatment without special therapy. The sick material observed consisted of 19 cases and 8 post-hemorrhagic anemias, 5 patients with achlorhydria (of whom one evidently had carcinoma of the stomach) 3 patients with hypochromic anemia with parasitic infection.

Of 15 patients 9 reacted well to liver diet in which processes there was no difference in therapeutic effect either with liver extract or liver feeding. In 3 cases better results were derived with liver diet than with iron and arsenic therapy. In a few cases the effect of iron and arsenic therapy was not augmented by liver dosage, in several cases iron and arsenic therapy succeeded better than liver therapy. The author comes to the conclusion that liver therapy in simple anemia should be tried in those cases which do not react to iron and arsenic, particularly in cases of post-hemorrhagic anemia and other conditions of long duration.

A Case of Post-Partum Hemorrhage. Medical Treatment. Cure. — Voron and Banssilon. (*Bull. Soc. obstét. et gynécol.*, No. 8 : 569, 1929.)

A case of a tertipara in good state of health, with sudden initiation of birth en route to the hospital, abundant lochia, from the 3rd day on intense hemorrhage with the elimination of large clots. The patient received injections of pituitary extract but only a very weak effect was obtained with these. Only with subcutaneous application of ergotamin was cessation first obtained. The patient left the hospital cured.

Fetus and Vitamin A. — E. Vogt. (*Münch. med. Wochenschr.*, **76** : 1748, 1929.)

Vitamins and endocrine glands are dependent upon each other. In rats keratomalacia occurs more promptly if one feeds thyroid gland substance simultaneously. The antisterility vitamin, E, and the ovarian hormone must be closely related for their activity is extensively dependent upon each other. Insulin and radiated ergosterin are

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very similar to each other physico-chemically. The author made tests on fetuses and found that Vitamin A can be determined in various stages of development in the liver in fetuses. However, Vitamin A was demonstrated in no other organ. From the exclusive presence and the storage of Vitamin A in fetal liver it is possible to estimate how important this organ is for vitamin metabolism in the fetal organism.

On the Question of the Possibility of Influencing the Effect of Thallium by Means of Extracts of Endocrine Glands, with Especial Reference to the Thymus. —Y. Vásárhelyi. (*Dermatol. Zeitschr.*, **56** : 412, 1929.)

The ingestion of active substances of the endocrine into the organism offers difficulties in that these substances are very sensitive to the salt acids of the stomach. In previous experiences the author observed that with the administration *per os* of fresh glands or of tablets no decisive effect could be expected and has therefore worked partly with extracts and partly with transplantation. The experiments were conducted on white rats; as indication of the effect of thallium the initial falling out of the hair was used. In animals which received besides 0.0002 gm. thallium daily, 0.5 cc. ext. testiculi or a similar dose of ext. ovarii, no influence of the sex gland extracts on the thallium poisoning was to be observed. In animals which received in addition to 0.0002 gm. thallium daily, 0.5 cc. of ext. thymus subcutaneously the falling out of the hair occurred much earlier than in the control animals treated with thallium alone and made definitely more rapid advances than in those thallium animals not treated with thymus extract. In the latter total baldness occurred on the 120th to 130th day, in the thymus animals on the 105th to 115th day. The author assumes that hyperthymization influences the effect of thallium positively. V. Berde came to the same conclusion. This condition explains also the observation that young organisms are considerably more sensitive to thallium.

Concerning Thrombosis and Embolism. — A. Mayer. (*Zentr. Gynäkol.*, **53** : 2770, 1929.)

It would be best to avoid thrombosis by means of prophylaxis. Unfortunately the mediums suitable are few and judgment of the effect is difficult. However, along with preliminary treatment by means of digitalization prophylactic thyroxin treatment also deserves consideration. According to Walters at the Mayo Clinic with 1745 patients under 70 years of age in large operations during two years no embolism was observed. The author gave no information on the amount of thyroxin treatment.

Is There a Form of Amenorrhea Which Can Be Caused by a Constitutionally Underfunctioning Thyroid Gland? — H. Toronczyk. (*Monatsschr. Geburtsh. u. Gynäkol.*, **83** : 167, 1929.)

A report on 12 cases of amenorrhea during the ages of 18 to 39 years, in which, regarding the genital findings it was to be assumed that barring the lack of menstrual bleeding, all other internal secretory functions of the ovary were in good condition. All 12 women were treated with thyroid and prompt success ensued. Most authors are in accord with the knowledge that the corpus luteum exerts a direct inhibiting effect, or as others believe, a neutralizing effect against thyroid. When the reformation of corpus luteum occurs and fails to exercise its inhibiting effect on the thyroid, as direct effect of this syndrome an initiating, always advancing intensification of thyroid gland activity must be assumed. If one takes the point of view that the stimulus to menstrual bleeding arises with the thyroid, the rôle of the corpus luteum at the commencement of pregnancy is clearer. Those cases of edema of pregnancy which are successfully treated with administration of thyroidin, can perhaps be caused by a too strongly developed mammary gland (hence a too strong inhibition of the thyroid gland). Cases of habitual abortion which were treated successfully with small amounts of iodin give evidence that in these cases there is a question of dysthyroidism. From experiments it is known that many dysfunctions of the thyroid gland can be influenced by small doses of iodin.

On the Effect of Several New Circulatory Mediums in Insufficiency of Blood Circulation. — P. Trendelenburg. (*Med. Klin.*, **25** : 1505, 1929.)

The insufficient heart can often be rendered promptly sufficient by means of ephedrin-ephetonin and the related adrenalin. The volume per minute increases, the auricular

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pressure decreases, heart dilatation ceases and the degree of resistance is overcome. That signifies, then, that ephedrin and adrenalin act on the insufficient conditions of the heart muscle fundamentally like digitalis and strophanthus glucoside; the difference lies in the promptness of the effect. The clinical results with adrenalin-ephedrin therapy in insufficiency of blood vessels is not so favorable as one would wish; hence true blood vessel insufficiency can hardly be remedied in human beings.

Disturbed Condition in Liver Therapy of Pernicious Anemia. — H. Taterka and Carl-Heinz Goldmann. (*Med. Klin.*, **25**: 1586, 1929.)

Only rather isolated reports (Ordway and Gorham, Davidson, McCrie and Gulland, Langstein) exist concerning secondary injuries with liver therapy. Four to 6 days after initiation of liver therapy in five cases of pernicious anemia, the author observed conditions of somnolence, extensive excitability and confusion. The clinical factor as a whole gave the impression of a dominant severe exacerbation. This condition lasted 2 to 3 days and then there was seen striking improvement of the general condition, with a very evident decrease of the anemia. The patient received liver up to a total daily amount corresponding to 1400 gm. of raw liver. The practical importance of the observation appears to the author to be the fact that an upset and collapsed condition occurs with the administration of particularly large amounts of liver, but this is not associated with any harm to the patient.

The Treatment of Ovarian Insufficiency with Sexual Hormone. — Harald Siebke. (*Münch. med. Wochenschr.*, **76** : 1752, 1929.)

All genital diseases which could likewise be improved with other remedies are unsuitable for the judgment of the success of hormone preparations. Along with the choice of cases, the choice of preparation to be administered plays a rôle. The sexual hormone has the best prospects and indeed, in the numerous clinical tests no harmful effect was ever observed when this hormone was used. The therapy with sexual hormone is not alone a substitution therapy, but often has a metabolic effect. The uterus once stimulated incites the ovary to increased activity by means of hyperemia of the pelvic layer, or the uterus, for example, in the treatment of amenorrhea, once initiated to menstruation after sexual hormone dosage, easily responds to the ovarian hormone stimulant in the future. Many times it is not necessary to continue the hormone treatment after one or two menstruations have been obtained. The therapeutic efficacy of the hormone preparation can be tested objectively in "growth tests" and in "tempo regulation tests." The growth test is positive if it is possible to make a small, underdeveloped incapable uterus, as the indication of vegetative ovarian insufficiency, a fully developed uterus which is capable of maintaining the monthly cycle and pregnancy; that signifies clinical improvement and cure of the symptoms evident through ovarian insufficiency.

The regulation tempo-test is positive if it is possible in amenorrhea, in cases of too seldom or too abundant bleeding as the sign of ovarian insufficiency, to induce a regular menstrual cycle, about every 4 weeks.

On the Significance of Endocrine Dermatoses in Woman. — M. Samuel and L. Strauss. (*Med. Klin.*, **25** : 1624, 1929.)

The prevalence of hyperglycemia is found in the climacterium, and if in young women, only in those with menorrhagias and painful disorders of menstruation due to ovarian dysfunction. It is relatively usual to observe an increase of blood sugar concentration during menstruation. This finding points, with apparent surety, to an endocrine relationship between the ovary and carbohydrate metabolism. In the majority of the authors' cases hyperglycemia was involved which was associated with the endocrine glands. These include such diseases as pruritus and intertriginous eczema. Insulin is recommended in these cases as well as in certain cases of menstrual disturbances (daily, 10 to 15 units of insulin for from several to 14 days) with relatively carbohydrate-poor diet.

Considerations and Facts of Endemic Thyroid Pathology. — W. Reyher. (*Würzburger Abhandl. Gesamtgeb. Med.*, New Series **6** : 179, 1929.)

The extraordinarily complicated pathology of endemic dystrophia with profound thyrogenous components, results alike in evidence of therapeutic success and of failure. In many cases it is possible to assuage the existing

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symptoms of insufficiency by means of thyroid gland therapy, as well as induce total subjective improvement. Objectively, however, one can determine the continuance of the vegetative and other components. The hypotonia, for example, remains unchanged. In other cases thyroid gland must be given with pituitary and sex glands in order to derive a reasonable result. In a large number of cases the therapy remains unsuccessful. In cases in which influenza preceded the thyropathia the author obtained important subjective improvement, that is, a totally healthy feeling, by the administration of thyroid gland tablets combined eventually with the administration of pituitary tablets and in all cases combined with Ca Ph (phytophosin). In individual cases, at any rate, recovery of the thyroid seems to ensue by means of the substitution therapy, even when it must seem to the physician that a relapse is imminent.

On the Polarization Capacity of Skin in Psychoses and Its Relation to the Function of the Thyroid Gland. — Ch. Roggenbau and W. Lueg. (*Monatsschr. Psychiat. u. Neurol.*, **78** : 301, 1929.)

From their investigations the authors draw the conclusion that in the disease picture of manic depressive irrationality, in contrast to schizophrenia, as a rule, thyroid gland disturbances play no insignificant rôle, and that a series of body symptoms, especially circulatory and metabolic disorders, which are to be seen in manic depressives, are dependent upon them.

On the Chemistry of the Pituitary Anterior Lobe — Sexual Hormone. — M. Reiss and F. Haurowitz. (*Zeitschr. ges. exp. Med.*, **68** : 371, 1929.)

The water-soluble preparations derived from the anterior lobe of the pituitary were disintegrated with weak concentrations of acids, with strong lye, with temperatures over 70° and also with oxidation mediums, for example, with 1 per cent H_2O_2. The raw preparation derived from the urine contains in addition to organic salts the amino-acids of the urine and "urine peptides." The author has accomplished the feat of binding this active substance to aluminium hydroxide or to the precipitation derived by means of uranylacetate, and thus to obtain a purification of three or four times. With regard to the control of the enzyme it is to be assumed that the hormone stands closer to the peptone than to the dipeptide. It is understood that the hormone is in large part inactivated by peroral administration. In order to derive the same effect as with parenteral dosage the oral dose must be increased 150 times. The hormone extracted from the gland in many ways resembles the substance from the urine. It is soluble in water and is obtained from this solution with alcohol and also is attacked in a similar manner by the proteolytic enzyme as the substance derived from the urine. From these investigations it must be concluded that the product derived from the urine is closely related to that of the anterior lobe of the pituitary.

Menstrual Dermatoses. — S. Recausens. (*Med. Welt*, **3** : 1497, 1929.)

Everything relating to the treatment of dermatoses during menstruation is still doubtful, and the results obtained in many cases of ovarian and pituitary insufficiency are very uncertain. The therapy with preparations from the ovary and its various components is to be preferred above all others. Unfortunately results have not been obtained in the beginning which would lend encouragement. Ovarian extract, corpus luteum extract, the hormone folliculin, "Tyro-Ovarin-ovarian pituitary hormone" have not caused the desired activity of the ovary in the majority of cases and have made possible the institution of increase of menstrual bleeding. Roentgen ray stimulation treatment of the ovary and pituitary in instances of insufficiency of these glands, must be tested, likewise transplantation of ovary may induce good results.

On the Influence of Thymus and Spleen Extracts on Calcium Metabolism. — M. Reiss, K. Winter and N. Halpern. (*Endokrinologie*, **5** : 230, 1929.)

On the basis of their experiments the authors come to the conclusion that: In short experimental tests, thymus extracts act invariably to decrease blood calcium content. Thymus extracts injected in longer processes, effect an increase of total calcium and a calcium enrichment of the bones. Spleen extracts act in the same way as thymus extracts. Extracts of muscle and liver are ineffective.

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Investigations on the Inhibition of Post-Operative Thrombosis and Embolism by Means of Ingestion of Thyroxin. —H. L. Popper. (*Med. Klin.*, **25**: 1588, 1929.)

In 150 cases treated with synthetic thyroxin, there were found a mortal lung embolism and three instances of thrombophlebitis with one lung infarct; 150 untreated cases exhibited post-operatively 4 instances of thrombophlebitis, no lung infarcts, no embolism. Synthetic thyroxin exhibits no harmful secondary effects in any case. Of 50 cases treated with natural thyroxin 2 cases of thrombophlebitis were found of which one was a non-fatal lung embolism; in the 50 control cases, 1 mortal lung embolism and 1 thrombophlebitis. After natural thyroxin in the amount of 3 mg. per day in several cases there resulted symptoms of thyroidism. Because a prophylactic effect of thyroxin ingestion with regard to the occurrence of thrombophlebitis and lung embolism is not observed in the experimental investigations of the author, he maintains that the administration of thyroxin for this purpose is not indicated.

Concerning the Administration of Hypophysin in Nephrolithiasis. — H. Naumann. (*Med. Klin.*, **25** : 1623, 1929.)

A report on the experiences with 50 patients. An effect with hypophysin is only to be expected if the calculus has already entered the ureter; the smooth musculature here, more abundant than in the pelvis of the kidney, reacts more promptly to hypophysin. The number of instances of elimination of calculi with hypophysin (three times in 50 cases) does not surpass the percentage of these cases in which spontaneous stone elimination occurred without artificial aid. The hypophysin method in differential diagnosis often fails, as one may expect from the theoretical considerations.

Concerning the Adrenalin Effect on Isolated Guinea Pig Uterus, Dissociated from Cycle Hormone. — M. Kochmann and H. Seel. (*Zeitschr. ges. exp. Med.*, **68** : 238, 1929.)

The uterus of the guinea pig gives evidence of various spontaneous forms of movement, and especially various reactions to adrenalin, according to the hormonal condition in which the animal is found. During estrus contraction always follows adrenalin application, that is 1 day previous and 4 days after. In non-castrated guinea pigs the adrenalin inhibition appears to be strongest in the interestrum.

Criticism of the Pharmacological Therapy of the Digestive Tract. — Paul Trendelenburg. (*Med. Klin.*, **25** : 1800, 1929.)

The inhibition of the intestinal vago-stimulus was made possible by means of adrenalin, but the effect of adrenalin in peroral dosage chiefly has a local influence on the mucous membrane. An increased sensitization of the intestinal musculature itself is best accomplished by the extract of the posterior lobe of the pituitary which affects the ileum and colon.

Experimental Researches on the Influence of Extracts of the Anterior Lobe of the Pituitary on the Genital Apparatus of Rabbits and on Milk Production. — P. Stricker and F. Grueter. (*Deut. med. Wochenschr.*, **55** : 1942, 1929.)

In rabbits in which ovulation had been induced, extracts of the anterior lobe of the pituitary led to rupture of the mature follicle and formation of corpora lutea which induced an effect on the uterus typical of that resulting from coitus. Extract of the anterior lobe of the pituitary exercises a noteworthy effect on milk secretion even after elimination of the ovaries (castration) so that the mammary glands are primarily prepared by the corpus luteum. On the other hand, it is easy to call forth these secretory indications again in animals (rabbits, female dogs) which have already delivered their young and no longer secrete milk. Finally, it is possible in castrated rabbits, even several months after castration and several weeks after total cessation of lactation, to obtain a reinstitution of milk secretion in quite small, retrogressed mammary glands.

The Experimental Basis of the Theory concerning the Mechanism of Action of Liver Diet Therapy. — Karl Singer. (*Wien. klin. Wochenschr.*, **42** : 1593, 1929.)

The experimental analysis of the mechanism of action of liver diet therapy has shown that in the symptom complex two factors must be differentiated. 1. A new blood formation and a blood decomposition-promoting impetus of non-specific sort, which is the property of liver as well as of flesh, but not of

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liver extract. 2. A specific principle which is also contained in liver extract and which is required for the production of valid red blood corpuscles in uninvolved perniciosa.

It is further demonstrated that the quantitative method of administration up to the present is not sufficient alone for the explanation of many problems of normal and pathological blood conditions, that more often the quality of the erythrocyte production must be considered. The biophysical and biochemical construction of red blood corpuscles is, however, an entirely unexplored realm. For the acquisition of knowledge, there is here, as usual, the urgent need of functional hematology.

Concerning Individual Effects of Parathyroid Preparations. — Anna Sucher. (*Wien. klin. Wochenschr.*, **42** : 1504, 1929.)

In a 62 year old woman suffering from painful condition of the bones, angio-neurotic edema, general debility and mental depression, prompt relief through parathyrin was obtained and also elimination of these symptoms. Not only parenteral, but oral dosage, too, was accompanied by the same success, a circumstance which is significant on account of the duration of treatment.

The Possibilities and Limitations of Liver Therapy. — R. Seyderhelm. (*Deut. med. Wochenschr.*, **54** : 1704, 1929.)

According to the present state of affairs as recorded in the literature, in most cases anemia is warded off as long as liver is administered. The singular fatal cases are explained as due to inadequate amounts of liver, calcium complications, toxic injuries of the central nervous system, intercurrent diseases (sepsis, pyelitis, pneumonia). The problem of dosage is very important, particularly at the commencement of treatment of very severe cases. At most 200 to 500 gm. of liver is required. Often by means of a "liver deluge" (up to 1200 gm. daily) in apparently refractory cases, too, an alteration in tone may be obtained. In such amounts the combination of peroral and rectal administration is recommended. The disappearance of urobilin and urobilinogen from the urine, the appearance of reticulocytes and the accumulation of hemoglobin and erythrocytes serve as first criteria for the effect, at the same time as control for the amplitude of the dosage. A sudden release of normoblasts with decrease of hemoglobin and erythrocyte values is the "desperate crisis of the bone marrow" suggesting a suspicion of carcinoma metastases in the bone marrow. The toxic symptom in the central nervous system, funicular myelitis, remains uninfluenced by liver therapy (few reports to the contrary). Hence, the disease picture is quite a new sort. After dropping off of the anemia the pernicious anemia is changed into a pernicious myeloencephalotoxicosis (hallucinations, severe disturbances of speech, coma with Kussmaul type of respiration). Hence liver therapy is not a causal, but rather a symptomatic therapy, directed against an established symptom complex.

Concerning the Action of Kidney Extracts on Functional Conditions of Kidney Contraction. — K. Stejskal. (*Med. Klin.*, **1** : 1015, 1929.)

After intracutaneous injection of 2 to 5 cc. of a watery kidney extract or a lipoid-containing extract, albumin-free, however, of this organ, a definite drop in blood pressure was observed in several patients with primary or secondary contracted kidney. The effect on the blood pressure is organ specific, that is it follows only after injection of kidney extracts (not after extracts of liver or brain) and only in nephritic hypertonics. The indication of an effect not only of albumin substances but also of lipoid extracts of the kidney on blood pressure has a practical as well as a theoretical significance. The fall in blood pressure can be spoken of as a direct effect of administration of the extract or as a secondary effect as a result of local vasodilatation of the kidney and hence associated improvement of the blood supply of the kidney. Perhaps there is a relation between the substances contained in the kidney extract and the Frey circulation hormone from the urine.

Book Reviews

"Rembrandt." By J. G. De Lint. Monograph Series of Great Painters and Their Works As Seen by a Doctor, Published by J. Philip Kruseman, The Hague, Holland. No. 1, 113 pages, cloth, $2.50.

This book contains a large number of reproductions of the paintings, etchings and

(*Continued on page 315*)

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drawings of the greatest of all Dutch painters — Rembrandt — of subjects relating to medicine and physicians. Some of the drawings are of the greatest interest to the physician as indications of Rembrandt's unequalled ability to preserve with a few lines his impressions and observations of subjects, doubtless material for future use in his finished works. His portrayal of the face in pain, emotion, sleep, and fatigue and the postural accompaniments of these states give evidence of his peculiarly well developed power of observation. Apparently the great artist's eye caught details perhaps overlooked by the physician whose thoughts were occupied not only with observing facts but in attempting to relate them to some of the involved theories of medicine of the time. (Perhaps too warm an attachment for a theory may have created a "mental hazard" in observing some facts on the part of the physician.) In the painting "The Lecture on Anatomy of Nicolaas Tulp" Rembrandt has portrayed the tendons of the flexor profundus digitorum perforating those of the more superficial flexor sublimis digitorum showing the insertions of each which make possible the flexing of the several phalanges. Extraordinary observations must have been supplemented by the advice of the anatomist himself in this case.

The textual matter gives one the feeling of familiarity with both the picture and with Rembrandt.

Pictures and discussions from medical subjects of the Bible and from every day life receive about equal treatment. To the physician who is a lover of painting the book is of extraordinary interest. To the physician who has not been greatly interested in art it will likely stimulate such an interest, for the subject matter is peculiarly the physician's own.

"Medical Art Calendar." Published by J. Philip Kruseman, The Hague, Holland, 1930.

This is the 1930 edition of the "Medical Art Calendar."

Each page contains a splendid reproduction of a work of one of the old Masters dealing with medicine. The description is in both Dutch and English. There are one reproduction and two weeks' dates to a page, and blank spaces for memoranda. It is a very artistic production and would grace any physician's office.

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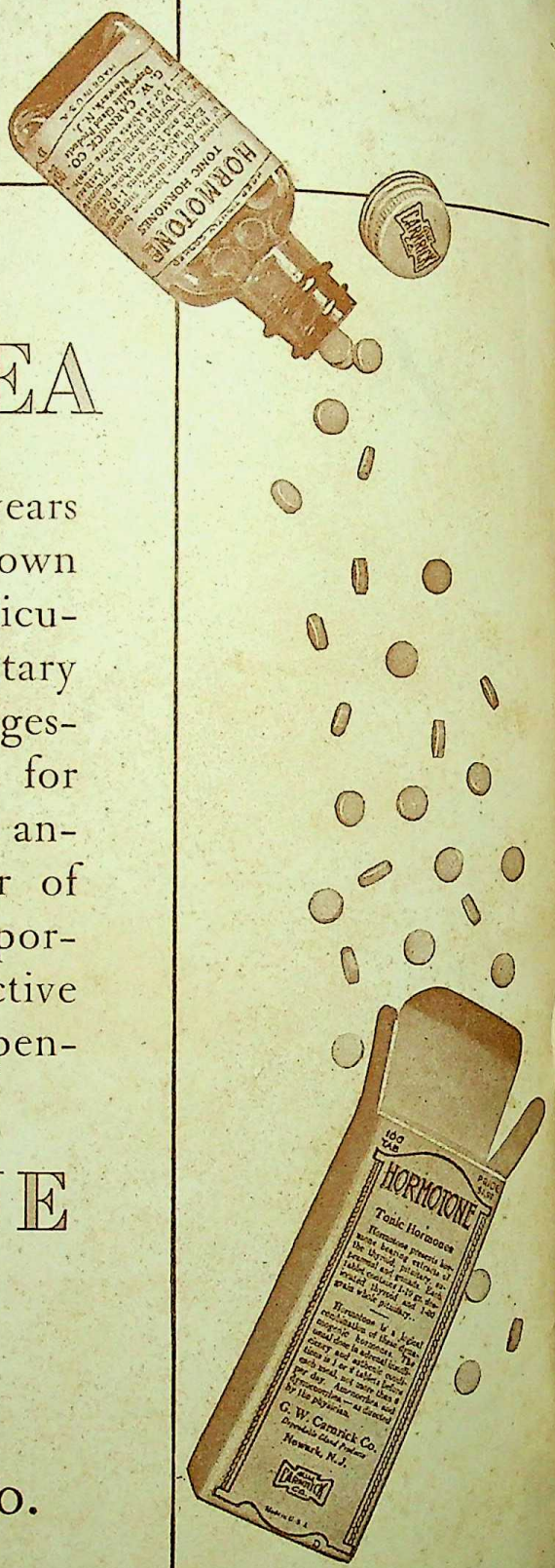
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Vol. XIV SEPTEMBER-OCTOBER, 1930 No. 5

The Journal of Organotherapy

A Record of Progress in the Study of the Internal Secretions and Metabolism

G. W. CARNRICK CO., *Publishers*

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Menstruation and the Hormones of Ovary and Anterior Pituitary

Clinical Observations concerning Respiratory Basal Metabolism

The Doctor's Page
Gregor Johann Mendel (1822-1884)

Medical Subjects by Famous Masters
"A Barber Surgeon Removing a Plaster from a Man's Foot"

Practical Therapeutics

Editorial Comment

Abstracts

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DYSMENORRHEA

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"The condition is, therefore, one of continual hammering at the patient's nervous system and eventuates gradually in seriously affecting it. It is no wonder, therefore, that the patients with dysmenorrhea nearly always in time become neurotic." (Prof. William Graves —Harvard Medical School.)

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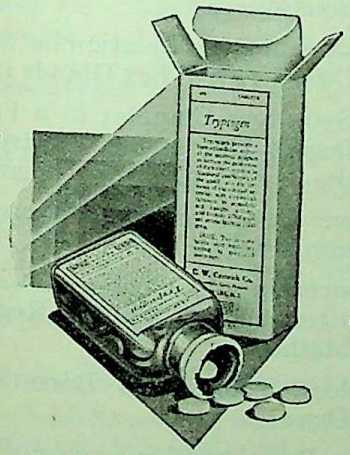
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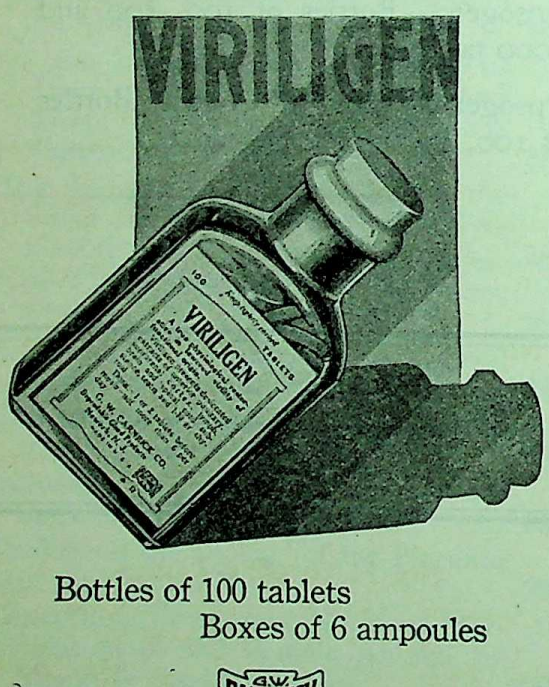
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Tablets 40, 100 Capsules 40, 100

Thyroid grs. 1/10
Pituitary grs. 1/40
Suprarenal grs. 1/4
Orchic grs. 1/4
Physiological Salts Comp. grs. 1/4

No. 2 Glandular Comp. Female

Hypoadrenia, Asthenia, Low Blood Pressure, Fatigue Syndrome

Tablets 40, 100 Capsules 40, 100

Thyroid grs. 1/10
Pituitary grs. 1/40
Suprarenal grs. 1/4
Ovarian grs. 1/4
Physiological Salts Comp. gr. 1/4

No. 3 Pineal Comp. Male

Backward Children, Mongolism, Retarded Mental or Physical Development

Tablets 40, 100 Capsules 40, 100

Anterior Pituitary grs. 1/5
Thyroid grs. 1/8
Suprarenal grs. 1
Orchic grs. 1 1/2
Pineal grs. 1/30
Physiological Salts Comp. grs. 1/4

No. 4 Pineal Comp. Female

Backward Children, Mongolism, Retarded Mental or Physical Development

Tablets 40, 100 Capsules 40, 100

Anterior Pituitary grs. 1/5
Thyroid grs. 1/8
Suprarenal grs. 1
Ovarian grs. 1 1/2
Pineal grs. 1/30
Physiological Salts Comp. grs. 1/4

No. 5 Orchic-Prostate Comp.

Enlarged Prostate, Sexual Neurasthenia, Vesical Irritation

Tablets 40, 100 Capsules 40, 100

Orchic grs. 1
Prostate grs. 2
Calcium Glycerophosphate grs. 2

No. 6 Corpus Luteum Comp.

Vomiting of Pregnancy (Hyperemesis Gravidarum), Menstruation Psychosis, Mild Manic Depressive Insanity (Female)

Tablets 40, 100 Capsules 40, 100

Corpus Luteum grs. 1
Thyroid grs. 1/10
Physiological Salts Comp. grs. 1/4

No. 7 Parathyroid Comp.

Tetany, Uremia, Epilepsy, Paralysis Agitans, Nervous Tremor of Children

Tablets 40, 100 Capsules 40, 100

Parathyroid grs. 1/20
Orchic grs. 1
Calcium Lactate grs. 2

No. 8 Thymus Comp.

Chronic Arthritis, Rheumatoid Arthritis, Arthritis Deformans

Tablets 40, 100 Capsules 40, 100

Thymus grs. 3
Thyroid grs. 1/10
Pituitary grs. 1/20

No. 9 Mammary Comp.

Menorrhagia, Metrorrhagia, Subinvolution, Prolonged Menses, Uterine Oozing

Tablets 40, 100 Capsules 40, 100

Mammary grs. 2
Thymus grs. 1/2
Posterior Pituitary grs. 1/10
Placenta grs. 1/2
Calcium Lactate, grs. 1

No. 10 Suprarenal-Pituitary Comp.

Asthma, Bronchial Asthma

Tablets 40, 100 Capsules 40, 100

Suprarenal grs. 2
Pituitary Entire grs. 1/2
Thyroid grs. 1/10
Anterior Pituitary grs. 1 1/2
Physiological Salts Comp. grs. 1/4

No. 11 Ovarian Comp.

Amenorrhea, Ovarian Hypofunction, Menopause

Tablets 40, 100 Capsules 40, 100

Ovarian grs. 3
Thyroid grs. 1/10
Physiological Salts Comp. grs. 1/4

No. 12 Renal-Pancreas Comp.

Nephritis, Prevention of Uremia

Tablets 40, 100 Capsules 40, 100

Kidney grs. 2
Pancreas grs. 2
Physiological Salts Comp. grs. 1/4

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NEURASTHENIA

"Many of the symptoms of physical and mental tire, with low blood pressure, especially if accompanied by increased pigmentation anywhere on the skin, may be due to an insufficiency of the suprarenals. * * * This whole discussion seems to show that the trouble is with the endocrine glands." (*Hand Book of Therapy*---O. T. Osborne and Morris Fishbein.)

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Menstruation and the Hormones of Ovary and Anterior Pituitary

MENSTRUATION in the human female is attended by certain definite developmental and degenerative changes in the endometrium. These changes depend upon at least two hormones arising in the ovary and two in the anterior lobe of the pituitary. It is not established that estrus in lower animals is equivalent to human menstruation.

DESPITE the indubitable position of importance of the menstruation process in female physiology, it has received remarkably scant attention, compared with other fundamental physiologic mechanisms until very recent times — practically until the last decade. This is somewhat astonishing for menstruation is indissolubly related to and bound up with the process of reproduction in higher animals and thus traces its origin far back in evolutionary history — its biologic necessity arising even with the appearance of the placenta in bisexual reproduction.

Again it is remarkable by reason of the enormous importance of abnormalities of this function in human disease, for there is probably no physiologic mechanism so subject to variations from normal or which demands so much medical attention.

Menstruation appears with and marks the beginning of the period of female puberty

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— the somewhat sudden appearance of fully developed sexual maturity. Indeed menstruation together with the changes in the ovary may be regarded as the important physiologic phenomenon of puberty. The ovary, as is well known, has a direct causal relation to menstruation: ablation resulting in absolute cessation of menstruation which may again be induced by transplantation of an ovary. This fundamental observation also established another vital point. The ovary exercises its control over the menstrual process by means of some substances elaborated into the blood and not by any nervous mechanism. Widespread research on the internal secretion or secretions of the ovary responsible for the changes of menstruation have resulted in some positive additions to our knowledge. The ovary elaborates at least two hormones, one the follicular or "Allen-Doisy" hormone and one the luteal hormone. Both, as will be seen, exercise fundamental and different effects on the process of menstruation. Within recent years another endocrine tissue — the anterior lobe of the pituitary — has been related to the process and there now remains no doubt that an anterior pituitary hormone is a normal and necessary factor in the endocrine mechanism controlling menstruation. This pituitary action seems almost certainly to be exerted through the intermediary of the ovary.

Another internal secretory effect and one of which less is known, is that produced by the ovum itself or the trophoblast formed by its implantation on the uterine mucosa.

These various factors have been interrelated in different schemes of action by several of the contributors to the field. It is not yet possible to formulate precisely the manner of interaction of these several factors, but there has been accumulated a substantial mass of facts relating to each of them individually. We can not assign a "cause" for menstruation from a closed cycle of interrelated factors. About all we can hope to do is accurately to establish the sequence among them and describe the details of the process. In the description of ultimate facts in any science, however, this is what we do. We can frequently describe the "how" but not the "why."

The structural changes taking place in the uterine cycle are described by Marshall (1) as follows:

"(1) The constructive stage.
"(2) The destructive stage.
"(3) The stage of repair.
"(4) The stage of quiescence.

"During the constructive stage the uterus undergoes growth, glandular development, and hyperaemia, *i. e.*, increase in the blood vessels, both in size and in number. The changes in a general way are described as being very similar to those which occur at the commencement of pregnancy.

"At the beginning of the destructive stage the congested vessels in the uterine mucosa break down, and blood is freely extravasated in the tissue. It subsequently forms large lacuna-like spaces in the superficial part of the tissue, and then the epithelium ruptures and bleeding takes place in the cavity. The whole, or a great part of the superficial epithelium, is removed as a result of the extensive haemorrhage, and a varying amount of underlying stroma tissue may also be torn away, leaving the lumen of the uterus bounded by a raw edge. The discharged blood, together with degenerate epithelial and stroma cells, constitute the menstrual clot, and this along with a sanguine-mucous flow passes down the uterus and through the vagina to the exterior. The amount of blood lost in a woman is on an average about three ounces, and the discharge lasts from three to six days. The uterine glands are active during menstruation and contribute to the discharge. When the tissue denudation is exceptionally great the condition is known as *menorrhagia*, and when it results in a painful condition it is called *dysmenorrhoea*.

"During the next period, repair sets in, the epithelium being renewed either from cells which did not suffer destruction in the pre-

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ceding period or from the cells of the glands. At this stage the blood vessels become reduced in size and number. The stage of repair is followed by a stage of apparent quiescence, but it seems probable that in many individuals the uterus commences to undergo growth changes which are continued in the succeeding constructive stage."

Now, what are the relations of the ovary and anterior pituitary to these cyclic changes in the uterus?

The purpose of the whole process is, of course, reproduction and we may begin with ovulation or the discharge of a matured ovum from the ovary. This event has been held to be essential to all of the succeeding changes in menstruation. Recently, however, evidence has been presented that tends to vitiate the importance of the ovum in the process (2), although, as will be shown later, the validity of this evidence is questionable.

"In spite of a great deal of circumstantial evidence of this sort, however, this theory of the essential rôle of the ovum in menstrual periodicity must give way, it seems to me, before certain facts which have apparently been established. One of these has already been referred to: the occurrence, at least in monkeys, of definite periodic bleeding with no sign of ovulation, and, for that matter, after apparent destruction of the entire follicle apparatus by roentgenization of the ovaries. In the case of some animals at least, there is some evidence, which, however, needs substantiation, that the sex cycle can continue after complete castration (Halban, *Zentr. Gynäkol.*, 35 : 1585, 1911). There have also been reports from time to time, especially in the older gynecologic literature, of the persistence of human menstruation after removal of both ovaries. Most of these, however, have been unconvincing, because of the ever-present possibility that ovarian tissue had been left behind, or that supernumerary ovarian tissue was present.

"A number of observers have reported that the tubes of an animal are ligated or excised so that the ovum cannot enter the generative canal after its discharge from the ovary, the sex cycle continues normally. This experiment is a rather obvious one from the human standpoint, for the same conditions and the same results are seen in the innumerable cases of salpingitis with completely sealed tubes, often necessitating excision. Such experiments do not, of course, eliminate the possibility of the continuance of a hormonic influence from the ovum even if it is lost in the peritoneal cavity. This factor can, however, be eliminated by allowing the ovum to enter the tube and then washing it out. The experiment has been done by a number of investigators, and even in the human subject evidence along this line is available in the work of Allen and his associates (Allen, Pratt, Newell and Bland, *J. Am. Med. Assn.*, 91 : 1018, Oct. 6, 1928), who first successfully removed human ova from the tube. In their cases, even though the ova were thus washed out, the sex cycle was undisturbed.

"Again, the recent studies of the results of anterior pituitary implantations on the ovary and the generative tract indicate that, even in immature animals, the phenomenon of estrus can be elicited by the simple impetus of the implantation, while the ova appear to play a rather passive rôle. These experiments would seem to establish that the ovum is not the underlying factor in menstruation, though they do not in themselves eliminate it as a factor in its periodicity.

"Finally, in the only report as yet available on the subject, that of Allen, Pratt and their co-workers, there would seem to be serious doubt whether the human ovum lives more than a short time after its discharge from the follicle. In all cases in which the ova were washed out from the tube, the operation was done at about the middle of the cycle, *i. e.*, only a few days after ovulation, and other evidence supported this belief. Yet all the ova already showed signs of definite degeneration. Certainly it would seem difficult to believe that the ovum can retain its vitality for

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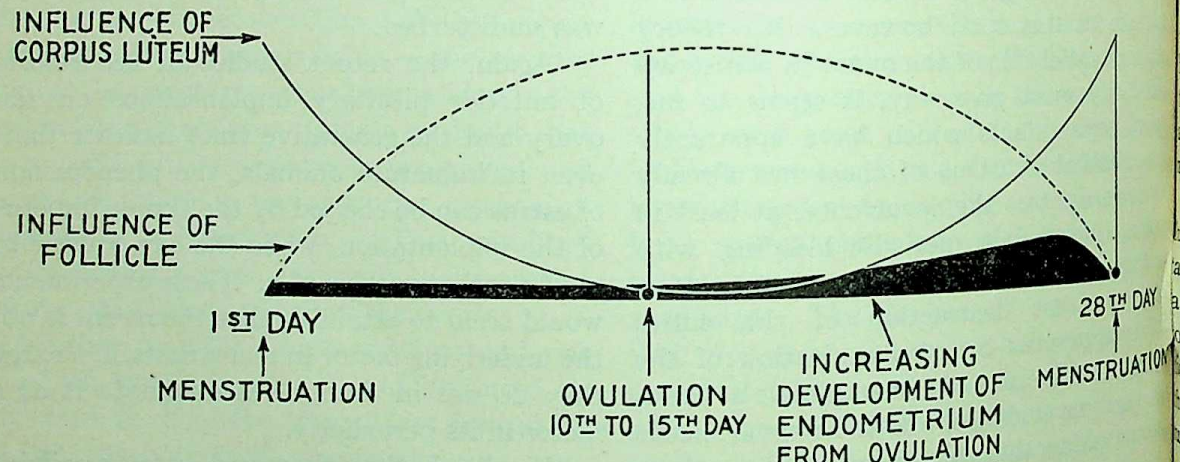
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the two week span formerly accepted. These observations are as yet too few in number to constitute an imposing array, but they must, with the other evidence I have mentioned, impel us to search for some other underlying factor than the ovum." (Novak (2).)

Ovulation takes place about the middle of the menstrual cycle, *i. e.* on the 13th or 14th day of the 28 day cycle. At the time the uterine mucosa undergoes hypertrophic changes suitable for the reception of the ovum. These changes have been gradual and began immediately after the last preceding menstruation. They correspond to the changes described under (1) constructive stage above. Immediately after the extrusion of the ovum the graafian follicle undergoes definite organization with the formation of a new type of tissue, the corpus luteum, and this gives rise to an internal secretion which plays an important and necessary part in the subsequent changes.

The influence of the internal secretion of the corpus luteum begins, therefore, in the intermenstrual period and increases up to the next menstrual period when it degenerates.

Another active internal secretion of the ovary, the follicular or "Allen-Doisy" hormone, also plays an essential, although entirely different, part in the process. This hormone is found (largely at least) in the follicle during development of the ovum and therefore exerts its action at a different period of the cycle. The time relationship of these several factors together with the development of the uterine mucosa is shown graphically in the diagram reproduced from this Journal (Vol. XII, No. 1).



We may inquire as to the nature of positive evidence of the presence of these several postulated hormones, the follicular and the luteal, from the ovary, two from the anterior pituitary and possibly one from the ovum itself.

Of the follicular hormone (folliculin, estrin or "Allen-Doisy" hormone) there can be no possible question. Prepared first by Allen and Doisy, and by Zondek and Laquer and later by a host of workers all over the world, its existence is indisputable. Precise biological assay is possible and its effects unmistakable. Frank and Goldberger have demonstrated the presence of this hormone in the blood of women and have shown that there is a cyclic accumulation in the blood reaching a maximum just before menstruation.

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In amenorrheic women this accumulation of hormone to a "threshold" point is definitely absent. The follicular hormone is estrus-stimulating. Moreover, in the light of recent research it seems to exert a necessary action on the endometrium, supplementary to the hormone of the corpus luteum in inducing the changes of progestational proliferation. This is important if it is true as proposed by Johnstone that estrus changes and reproductive changes are two different processes. While such an effect supplementing the action of the luteal hormone in the endometrium makes the follicular hormone a factor in menstruation of the human type and in which the influence of the corpus luteum is indispensable it should be noted that it is primarily a hormone inducing estrus, which may be an entirely different phenomenon from menstruation. Thus its chief effects (at least in lower animals) are related to changes in vaginal epithelium rather than the uterus — the method of its assay by Papanicolaou and Stockard depending on this fact. The uterus, however, shows some hypertrophic changes, which require the additional effect of the luteal hormone to bring about the decidua characteristic of true menstruation.

Concerning the hormone of the corpus luteum there would seem to be no less certainty than of that of the follicle. Much of the earlier work suggestive of a definite luteal hormone was based upon the constant relation of the development and degeneration of the corpus luteum to the uterine changes resulting in menstruation.

In animals extrusion of the corpus luteum by squeezing hastens the estrous period. Persistent corpora lutea suppress ovulation and their expression results in reappearance of estrus. In the human female persistent corpus luteum inhibits menstruation. Much evidence of this kind is available. Further proof of a luteal hormone has been presented in the preparation of active luteal substances exerting definite estrus-inhibiting effects. Papanicolaou (3), Parkes and Bellerby (4) and Allen (5) have been entirely successful in preparing such extracts. The action of the luteal hormone is described by Papanicolaou as follows:

"The proper luteal hormone and the female sex hormone act in an entirely different way from each other and are, to a certain extent, antagonistic. The luteal hormone inhibits and delays ovulation and estrus, whereas the female sex hormone rather accelerates these processes to a limited extent. The luteal, in a purified state, does not excite estrus and does not cause hypertrophy in the genital tract of spayed females, as the female sex hormone does to a striking degree. Both are active during pregnancy, but act in different manners. The one inhibits, the other stimulates. The two, however, act simultaneously. The oral administration of extracts containing luteal hormone gave no results, though large doses have been used. From a practical point of view, this method of administration cannot be utilized at present."

More recent work on the subject, however, casts some doubt on the antagonistic relationship between the two hormones. Rather, it would appear that the corpus luteum supplements and continues at a later period the effect of the follicular hormone of an earlier period. This point of view is presented by Hisaw and Leonard (6).

"From the data presented in this paper it seems quite clear that the progestational proliferation characteristic of the rabbit uterus during pseudo-pregnancy is the result of a combined effect of follicular and corpus luteum hormones. The function of the follicular hormone seems to be that of putting the uterus into proper physiological condition so it can respond to the corpus luteum hormone. Neither of these substances can produce progestational proliferation in the castrate uterus when given alone. If, however, the castrate uterus is first brought into the condition typical of oestrum through the injection of follicular hormone and is followed immediately by corpus luteum treatment, progestational

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proliferation results. It also seems that a quantitative relationship between the follicular and corpus luteum hormones must exist for the prolongation of the progestational picture over an extended period."

Allen (7) and Allen, Pratt, Newell and Bland (8) give a similar conclusion. Weichert (9) found that progestational proliferation can be induced by the luteal hormone if the follicular hormone has previously been injected, but only a negligible number respond to the corpus luteum alone. He sensitized the uterus of the unmated rat in the diestrous cycle by corpus luteum extracts as well as ovariectomized animals in which estrus had been induced previously by injection of the follicular hormone.

The influence of the hormone of the anterior pituitary has been demonstrated more recently. Although some correlation of function between the pituitary and ovary had been suspected as a result of clinical observation and physiological changes, the actual demonstration of an active hormone, extracted from the anterior pituitary and exercising definite effects in the ovary, was first made by Evans (10). His experiments showed that the anterior pituitary hormone in addition to growth-promoting effects suppressed estrus and induced luteinization of the graafian follicles without preceding ovulation. The ovaries therefore showed larger number of organized and luteinized corpora lutea with vestiges of ova still remaining.

Teel (11) extended these observations and gave evidence of the effects of anterior pituitary hormone in producing corpora lutea which were functional in producing placentoma as first described by Leo Loeb.

"1. Under the conditions described, the daily injection of anterior hypophysial fluid always brings about a typical decidual cell response to injury of the uterine mucous membrane in animals in which the ovaries are present.

"This response does not occur when the ovaries are absent."

Smith (12) by transplantation methods further demonstrated the pituitary-ovary relationship.

"Daily homoplastic transplants of the pituitary from the adult, given intramuscularly, induce sexual maturity in the female rat as early as the weaning date (22 days of age), thus transcending all normal variability. Animals which are but fourteen days of age when treatment is begun mature sexually in from eight to ten days; when treatment is begun at the weaning date they mature in five to six days.

"The opposite response of the sex apparatus results from pituitary ablation before sexual maturity, the complete establishment of the vaginal canal being delayed and the genital system remaining undeveloped.

"2. The anterior pituitary component of the transplant only, is essential for the induction of premature sexual maturity, the posterior lobe of the pituitary neither hindering nor aiding in the response.

"3. No stimulus to the development of the uterus or vagina of the immature ovariectomized rat is given by these transplants.

"4. The invariable and rapid maturity which is induced by daily pituitary transplants speaks against the view of those who maintain that hypophysectomy does not interfere with sexual development or function, and indicates an important hypophyseal-gonadal interrelationship."

Zondek (13) finds that the anterior pituitary produces a growth hormone, concerned with the somatic growth (also reported by Evans and Simpson) and two sex hormones (or at least there are two factors bound up in the sex hormone). He calls them A and B. The first is concerned in maturation of the follicle and the second in causing luteinization. The A factor is not characteristic of pregnancy and may occur in the urine in non-pregnant women. The B factor has been constantly demonstrated in the urine of pregnancy and Zondek and Aschheim have developed a test for pregnancy on this basis.

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Hormone from the urine of a pregnant patient is injected into immature female mice and gives characteristic changes in the ovaries.

Zondek and Aschheim (14) also made implantations of the anterior pituitary of mice and succeeded in inducing early estrus. They concluded that the effect was exerted only through the ovary which undergoes early maturation and elaborates follicular, estrus-inducing hormone. Now, whereas Zondek and Aschheim, and Smith clearly showed induction of precocious sexual maturity, the ripening of the large number of graafian follicles and ovulation, Evans, as noted above, found suppression of ovulation and luteinization of the follicles leaving the ovum imbedded in the follicular mass. This discrepancy is doubtless due to the different methods of supplying the hormone of the anterior pituitary — implantation and injection. Evans and Simpson (15) describe this as follows:

"Precocious maturity had been secured by the implantation of perfectly fresh warm rat glands; growth by the administration of various extracts of 8 hour old bovine glands. The markedly different results from these two procedures could have been due to the freshness or staleness of the glands used, the source of the glandular material (rat or bovine), or the method of preparation of the material. We can show that the latter explanation is the correct one. Both hormones reside in the anterior hypophyseal tissue from either source, rat or bovine, and specific extractives can be used for either. The growth hormone cannot easily escape from the relatively large tissue fragments used in the implantation method, but it can readily do so when this tissue is merely triturated, and extraction of rat glands in a way identical with that employed in the bovine growth extracts showed a similar abundance of the growth hormone in the tiny glandules. If the implantation method is employed (*i. e.*, whole rat or similar sized portions of bovine glands introduced intramuscularly), double the weight of substance essential for satisfactory growth extract will not confer growth. On the other hand, implanted bovine glands stimulate precocious sexuality as do rat glands and but little diminution in this hormone occurs with six hours "aging" after the death of the donor. It has furthermore been possible for us to secure the maturity-provoking or sex-stimulating anterior hypophyseal hormone by extracting this tissue in ways different from that employed for the growth hormone, and successful extracts of the second hormone had been employed by us before the very recent publications of Zondek and Aschheim (*Klin. Wochenschr.*, 7 : 831, Apr. 29, 1928) indicating partial purification of this substance."

Without question these and other experiments prove that the anterior pituitary acts through the ovary and not directly on the uterus. Moreover, the factor initiating the ovarian changes is not resident in the ovary itself but in the anterior pituitary.

The Ovum and Menstruation. — It has been shown that the anterior pituitary exerts a primary influence in causing ovulation and the subsequent ovarian changes, and without doubt in normal human menstruation this constitutes the regular scheme. Nevertheless, in the menstruation of monkeys Corner (16) and Hartman (17) have shown that monkeys with apparently normal menstruation presented no signs of a preceding ovulation, of a graafian follicle or of a corpus luteum. Against this is the criticism of Robert Meyer that this type of bleeding in monkeys is not analogous to menstruation in women. Corner describes this type of bleeding (menstruation?) as not associated with the characteristic progestational changes of the endometrium resulting from a corpus luteum.

"In young mature females of the monkey, *Pithecus* (*Macacus*) *rhesus*, menstruation frequently occurs without ovulation, and is therefore not dependent on the presence of a corpus luteum. However, when ovulation occurs, it seems to take place at a definite time, about twelve or fourteen days before the onset of menstruation. Menstruation without

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ovulation is not preceded by the so-called premenstrual changes of the endometrium, which occur only after formation of the corpus luteum. The cause and meaning of menstruation, in this species, are not at present known."

R. W. Johnstone (18), as well as Meyer, holds that the cyclic bleeding of monkeys is not analogous to human menstruation. His views as to the independence of estrus and its changes from the reproductive function of which menstruation is a part are as follows:

"In approaching the subject, the first point which requires to be clearly apprehended is that in all female animals the generative organs, taken as a whole, have two distinct functions to subserve. One is the sexual or copulative function, whereby the female receives the male gametes into her genital tract; and the other is the reproductive function, which begins with ovulation and includes gestation, parturition, and lactation. We must keep these two functions quite distinct in our minds, for upon that distinction depends our understanding of the problem. In the lower mammals both the sexual and the reproductive functions occur at regularly recurring intervals, so that we have what we may call a sexual cycle and a reproductive cycle, each essentially distinct from the other.

"The sex cycle of the lower mammals is characterized by the regular recurrence of periods of estrus or sexual desire, and for the performance of the sexual act the genitalia of the female require special preparation. The opening of the vagina becomes enlarged, the vaginal epithelium becomes cornified, the uterus becomes enlarged and congested, and the secretions of the genital tract become increased — all with a view to the reception of the male gametes and to facilitate their swimming up into the oviducts. After the sexual congress, which almost inevitably occurs at this period in animals living in a state of nature, the genitalia begin to regress, and in some species there is actually a sanguineous discharge at this regressive stage, due to the congestion of the whole genital tract. It was the regular recurrence of this discharge, along with the other phenomena, which has led to its being generally regarded as the analogue of menstruation in the primates and in the human female; and while the analogy is tempting, I believe it to be incorrect.

"The second or reproductive function begins with the maturation and dehiscence of the ovum, and in all mammals ovulation is followed by a series of changes in the ovary and the uterus, designed to prepare for the nidation and gestation of the fertilized egg or eggs, changes consisting in the development of the corpus luteum in the ovary and in the vascularization and sensitization of the endometrium of the uterus and its metamorphosis into what we call the decidua. If the fertilized egg is forthcoming, and in the lower animals living in a state of nature it may be assumed that it almost always is, the reproductive cycle continues over the period of gestation and lactation and ends by the return of the ovary and uterus to their 'resting' condition, in readiness for the repetition of another reproductive cycle."

Johnstone believes therefore that bleeding alone does not constitute menstruation and that the ovum is a necessary link in the endocrine chain causing menstruation:

"I submit that the link must be some hormone formed by the trophoblast of the young ovum and that this in all probability stimulates the corpus luteum not only directly but through the medium of the anterior lobe of the pituitary body."

The entire process of menstruation and its several factors may now be briefly considered. Since the ultimate aim of the whole process is obviously reproduction it does not seem difficult to regard the cyclic menstrual flow and preparation of the endometrium as a result of failure of impregnation and it is now common to regard it as a pseudo-pregnancy. Every element proceeds just as if a

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real pregnancy were to occur and in the absence of impregnation the preparatory stages are discarded and preparations made for the reception of a new ovum. The process then is essentially a pseudo-pregnancy. The relationship of this process to estrus of the lower animals is made clear. According to Johnstone (quoted above) menstruation is not at all analogous to the bleeding of this pre-estrus, and "is essentially free from any causal connection with any trace of an estrus cycle."

The pseudo-pregnancy theory, of course, presupposes ovulation and the subsequent influence of the corpus luteum and since Corner's observation of menstruation (?) without ovulation (and corpus luteum influence) does not seem definitely to identify the bleeding of monkeys with menstruation in the human female (see his description of the process above), it would seem that the pseudo-pregnancy theory is still tenable. The changes of estrus are characterized by changes in the external genitalia and vaginal epithelium which bleed when the period of engorgement has passed. It does not appear that this type of bleeding is sufficient to identify it as menstruation which in the human female is characterized by a very definite development of the endometrium from which the bleeding later occurs.

Since the anterior pituitary is the "motor of the ovary" we may start with it in following the process. Two hormones are formed there: one exerts an action on maturation of the follicle and one on luteinization and growth.

The first pituitary hormone stimulates maturation of the follicle and ovulation and there is a large production of the follicular hormone. The follicular hormone accumulates in the body and exercises a sensitizing influence on the endometrium, and a cornification of the cells of the vagina. The second pituitary hormone acts on the graafian follicle following ovulation and luteinizes that structure, which then elaborates the luteal hormone. The luteal hormone represses further ovulation or maturation during the latter half of the 28 day cycle and further acts on the endometrium (first sensitized by the follicular hormone) exerting an effect of development and preparation for the ovum. The luteal effect and the hypertrophic, endometrial, progestational development proceed together and just before menstruation the corpus luteum degenerates and the hypertrophic endometrium likewise undergoes retrograde changes, bleeding, and sloughing off and a new cycle begins. During the whole period there is apparently an increasing concentration of follicular hormone which reaches the maximum just before menstruation. It acts as a supplement to the luteal hormone in preparing the progestational changes of the endometrium, induces estrus changes in the vagina, and apparently finally, at its point of greatest concentration has some part in inducing the degenerative changes preparatory to the menstrual flow (perhaps both on corpus luteum and on the endometrium. If this is true it is in effect antagonistic to the corpus luteum but is able to destroy it only when present in maximum concentration. Its action on the endometrium earlier, however, is necessary to supplement that of the corpus luteum.)

The interaction of the several hormones of the anterior pituitary, ovary and perhaps of the trophoblast of the imbedded ovum become practically certain. The mechanism begins to be vaguely understood, but much work remains before it can be precisely formulated.

1. Marshall, F. H. A., "An Introduction to Sexual Physiology," Longmans, Green & Co., London, 1925.
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(*Concluded on page 306*)

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Clinical Observations concerning Respiratory Basal Metabolism

(Translated from the article by Prof. F. de Quervain and Dr. F. Pedotti, First Assistant Physician at the Surgical Clinic, Berne.)

(*Mitteilungen aus den Grenzgebieten der Medizin und Chirurgie*, 39 : 646, 1926.)

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(Continued from Vol. XIV, No. 4)

If cretins generally show a metabolism slightly lower than cases of acquired myxedema, it must be recalled that, as mentioned, the metabolism values obtained from these are rather too high. On the other hand, it is clear that with them conditions obtain which are different from those in acquired myxedema. In the case of cretins we have before us, from childhood, a partial progressively defective thyroid gland with which the organism has plenty of time to accustom itself and certain compensation can be reckoned theoretically. However, despite the elimination of the more severe cases in which metabolism could not be tested, the fact that the average value lies so far under the normal at once shows us (in agreement with the histological findings) the importance of the thyroid gland insufficiency for the disease picture of cretinism. We stress this therefore, since from various sides, most recently from Finkbeiner, the pathogenetic importance of the thyroid gland defect for cretinism is always more or less doubted, even, is not accepted.

Up to the present the experiments undertaken on cretins have been concerned chiefly with albumin and mineral metabolism, while the investigations on the gas metabolism of endemic cretins is still totally lacking. In accordance with the case of cretinism investigated by Magnus-Levy it may be said that the individual had practically no thyroid gland, so that it was really a case of sporadic athyrosis. The work from the Koch Clinic is likewise concerned with albumin metabolism. In his enlightening experiments on the metabolism of albumin and minerals Scholz comes to the conclusion that perhaps cretinism lies "behind the myxedema" and that the oldest cretin behaves indifferently toward myxedema. With a view to the gas metabolism, one can say, in the main, that many cretins have never passed through the myxedema in the strict sense of the term, but by their own efforts they have corrected their metabolism for the disposal of the existing thyroid function.

In two cretin cases the *iodin* action and the *thyrakrin* action were checked. The results were as follows:

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O. M., 30 yrs. old, goiter cretin, not operated. Basal metabolism.	H. F., Male, 13 yrs. old, half cretin, Str. nodosa parenchymatosa. Basal metabolism.	W. M., 14 yrs. old, female cretin, not operated. Basal metabolism.
31/5/22 ..... −16% 4/6/22 ..... −31% 22/6/22 beginning of iodin cure, 0.05 potassium iodid per day. 28/6/22 ..... −0.68% 7/7/22 ..... −3.4% 8/9/22 ..... −2.2% Thus a strong influence of the intense minus value.	31/10/22 ..... −0.7% From hence 0.1 potassium iodid per day 7/11/22 ..... −2.2% 14/11/22 ..... −3.7% Thus no influence on the gas metabolism. The slight fall arises from improvement in the use of the apparatus.	16/6/22 −22.4% From 21/6/22 on 1 tablet of 0.3 Thyrakrin Oswald per day. 29/6/22 −10.9% 6/7/22 −0.7% Thus strong influence of the minus quantity.

We do not wish to draw any extensive conclusion from these isolated investigations. After all the presentation of these facts confirms the results, in accordance with the opinion of de Ligneris and partly agrees with the report of Breitner, that iodin mobilizes the thyroid secretion. The negative result in the second experiment may arise from the colloid impoverization of the gland and from the brevity of the experiment, especially considering the small dosage in so short an interval. The test should be tried again.

That thyroid gland preparations increase the gas metabolism is a fact well tested by an abundance of exact, quantitative experiments on thyroxin, performed in the laboratory of the Mayo Clinic. The example cited here illustrates the importance of the B. M. determination. The influence of thyrakrin was not such as to detract from the pulse frequency or the volume per minute, for apparently neither was influenced. The volume per minute even decreased after familiarization with the apparatus!

5. Cretinism without Goiter

In cretins without goiter we find exclusively minus values, yet even in these instances, four times, we find values between null and −10 per cent, thus lying in the valid region. Here, too, mention must be made that the values are too high, for the cretins lacked comprehension for the experiment and that most of the worst cases could not be investigated.

In cretins without goiter the thyroid gland is atrophic, histologically, but even at that, in the tests on tadpoles (Branovacky and Branovacky-Pelech) have shown us, it is not inactive. It is not sufficient because of the small volume, but it does perform a little, so that it is not necessary for these patients to experience the myxedematous stage. Nevertheless, this stage is often rather pronounced and lasts a long time. We have then to deal with various quantitative degrees and qualitative forms of insufficiency in which, perhaps, extra-thyroidal compensation processes also can be instituted. As the stereotype picture of the athyroidal individual indicates, these are quite inadequate. The total disturbance is on the average more severe than in goiter-bearing cretins, who often possess, besides the remaining atrophic gland, a certain amount of partially functioning goiter tissue for the process.

In the case of dwarf cretins the question may ultimately be raised whether the standard values can be employed off-hand in these cases. From the systematic investigation of dwarfs in whom the disturbance of growth has nothing to do with the function of the internally secreting glands, this can be determined. Such experiments have not yet appeared, however, and are not easily obtained in sufficient number for the cases are rare. The two cases of dwarfism investigated by Stähelin and Gigon are not free from objection as regards the thyroid gland, and therefore can not be applied comparatively.

We shall take up this point again elsewhere and we shall discuss in a special section the rôle of the body length in the determination of gas metabolism results, as applied to our particular material.

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6. Operated Basedow Cases and Common Goiter

This group contains some seven cases of Basedow, operated from 1-13 years previously, of various geographical distribution, whose average basal metabolism was −5.1 per cent, with limiting values of +4.7 and −9.1 per cent. The other average values are: Pulse 70, volume per minute 5.2, respiratory quotient 7.7, quite normal values. Two cases of common goiter, operated several years previous, with slight symptoms, indicated a basal metabolic value of −14 per cent and −15 per cent. In these nine cases the gas metabolism determination was not made before operation.

To this group may be added several comments concerning the *consequent experiments on Basedow goiter and various other struma previously tested by us.*

In Basedow goiter, the basal metabolism in nineteen controlled cases after tissue reduction operations, runs from an average of +36.6 per cent down to +7.9 per cent, thus signifying an average reduction of 28.7 per cent. Total ligature and then rest in bed for 14 days resulted in a significant, though slight decrease. A drop from +71 to +21 per cent was observed after 14 days rest in bed and the administration of 2-5 mg. iodin per day. We waive any claims here to the average results obtained because the experiments are so few and because a great amount of material has been observed, particularly in the American clinics (Mayo, Crile, etc.). Our material merely confirms what is already known.

In the matter of common goiter, only six cases were checked after operation and there was found, on the average of 30 days a drop of about 7.8 per cent.

In cretin goiters two checks were done which gave decreases of 1.1 per cent and 11.2 per cent. In both these cases we had to abandon the follow-up experiment for the reason that we had to dismiss the patients on other grounds — lack of room — usually a week after the operation, *i. e.* too soon to render them suitable controls.

7. Diverse Cases

Under the thirty-four diverse cases we have differentiated three sub-groups which have a particular interest, namely they are cases with *hypogenitalism*, *genuine adiposity* and *neurasthenia*. The remaining cases are divided according to various pathological conditions.

(*a*) *Male Hypogenitalism*

This group contains seven cases of underdevelopment of the external genital organs, from 11-55 years of age, belonging to the adiposogenital type, with vast fat deposits. Hypophysials in some normal, in some small. The average values are: Pulse 76, volume per minute 5.8, R. Q. 0.80, B. M. −10.95. These findings agree with those of Means, Marañón and Carrasco, Tierney and others, while Plant, Liebesny and Schwarz, Zondek and Löwy find partly normal values in their fat experiments in hypophysials. In these cases it is difficult to keep the direct influence of the hypophysial glands separate from that of the atrophic sex gland. The experimental researches of Asher and Bertschi on rabbits found no impression of the sex glands on the respiratory metabolism. According to Korentschewsky, one must assume an indirect association concerning the thyroid gland, while the removal of the sex glands remains ineffective, with coincident removal of the thyroid, with the presence of the latter, in contrast, the respiratory metabolism is lowered.

(*b*) *Female Adiposity*

This group embraces seven cases including two border cases. Four female patients from 11-22 years of age, all southern European origin, present a concordant aspect: Tendency to lay on fat, easily fatigued, mental apathy, and also signs of nervousness. Average intelligence, non-myxedematous type. The average values are: Pulse 72, volume per minute 5.4, R. Q. 0.79, B. M. −20.5. The basis for this condition may well lie in the

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thyroid gland, though we have no anatomical foundation for this assumption. Thyroid gland preparations seem to have a favorable action. Marañón assumes in such cases as these, a pluriglandular disturbance in which the ovary and thyroid glands play a leading rôle, and designates it as "juvenile ovary insufficiency." These cases deserve to be observed for a long time for their respiratory metabolism.

Included with these there are: One case of obesity in a 25 year old woman, from the south, with a B. M. −8.4 per cent, who can hold place in the above group, a case of common obesity with B. M. +8.7 per cent and a female case of adiposogenital type with B. M. -10.7 per cent. (In this case also, perhaps, there is thyroid gland insufficiency: Struma cystica, little healthy thyroid gland tissue.)

(c) *Neurasthenia*

This group contains five cases with basal metabolic values within normal limits (−3.9), indeed, with a pronounced tendency towards the minus side. In this instance, however, the volume per minute and the respiratory quotient show nothing particular.

(d) *Remaining Cases*

The following may be emphasized as interesting concerning the remaining cases called "varied."

One case each of *Little's disease* and *Parkinson's disease*, both with +14.7 per cent, which is not to be wondered at considering the muscular activity.

One case of *iodin idiosyncrasy*, one of *Morbus Darier*, one of *dermatitis herpetiformis* with normal values (−0.5 — +6.4 per cent).

One case of *scleroderma* with histologically normal thyroid gland: −11.0 per cent.

Two cases of *infantilism* which had been treated with thyroid gland preparations, with +4.3 and +4.7 per cent.

One case of *climacteric complaints* and puffiness, without evident myxedema, with +4.3 per cent (tested during treatment with thyroid gland).

A *constricting struma in a case of 8-months pregnancy*, with stridor: +30.9 per cent, in which case tracheostenosis and pregnancy were participating to increase the basal metabolism value.

A *proliferating struma according to Langhans* with +41 per cent, which dropped to −11 per cent after operation.

Finally, one case in this group deserves particular mention for it does not entirely fit into any other.

Female patient of 36 years, qualified as tachycardia, struma, slight exophthalmos, treated for 2 years as a Basedow case. When she came under investigation there existed a certain degree of exophthalmos. Further Basedow symptoms were lacking, however. The struma was diffuse with small nodules non-pulsating, horseshoe-shaped, slightly constricting. The patient was unexcited, quiet, somewhat phlegmatic, complaining of lack of energy. B. M. −6.6 per cent, after 5 days, calculated again, B. M. was −6.4 per cent. Operated for tracheostenosis. Histological finding: Struma colloides nodosa et diffusa. Chronic thyroiditis. In the tadpole experiment (Case 6 of Branovacky) the thyroid gland was quite active, Basedow-like.

Here we have to deal with a veritable dissociation of symptoms and with a combination of hyper- and hypo-symptoms. Was the case just about to pass from the first to the second stage? Why did the exophthalmos, still not anatomically fixed, have to lag behind? In this instance the assumption of a "mixed dysthyroidism," an inadequate association of secretion components can not be entirely rejected. After a year's time there was still exophthalmos. B. M. −14 per cent. Subjective improvement after treatment with thyroid gland.

8. Adolescent Goiter

In the material thus far reviewed, there are twenty-seven cases of struma from 12-18 years of age and one each of 9, 10 and 11 years. For these last three cases the standard

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values were calculated according to the Benedict determination for somewhat older children and hence the values are only approximate. If we consider these adolescent goiters in the same manner as the collective material, according to their *clinical* aspect, thus we find that

(*a*) For the 15 clinical euthyroid cases, B. M. +0.3 with limiting values of −9.6 and +15.3 per cent.

(*b*) For the 14 cases clinically estimated as hypothyroid, −12 per cent with limit values of +1.3 and −39.8 per cent.

(*c*) For the single Basedow case, +31 per cent.

Hence the average values are similar to those of the total material and we must conclude from this that the fate of incipient goiter cretins is as a rule determined several years *before* puberty.

Concerning the *histological character* of the struma we find in

	Euthyroids	Hypothyroids
Struma colloides diffusa	2	—
Struma colloides nodosa, *i. e.* diffusa and nodosa	—	—
Struma parenchymatosa diffusa	3	1
Struma parenchymatosa nodosa, *i. e.* diffusa and nodosa	1	1
Struma colloides nodosa	—	—
Struma parenchymatosa nodosa	5	9
Mixed forms	2	1
Non-operated: diffuse	1	1
nodular	—	—
mixed	1	—

We find here, too, as in our collective material from the district of Bern, a numerical predominance of struma nodosa parenchymatosa. The mother form of this, the struma parenchymatosa diffusa, in a narrow sense the adolescent goiter, is, indeed, as we must accept from the investigations in the schools, much more prominent, as such, however, it seldom requires operation since it is mostly adaptable to iodin therapy and since it causes tracheal stenosis only exceptionally. It is to be emphasized that there is greater percentage of the purely or predominatingly diffuse forms in euthyroids than in hypothyroids (46 per cent as against 21 per cent) and that in the latter cases the colloid forms do not occur. Lastly, I do not put much stock in the small number of cases. For the study of the early stages of cretin goiters we confine ourselves to the years *before* puberty. We shall touch upon this point again in another place and merely recall the gas metabolism experiments made in our clinic by H. Doubler in 1920-22 on cases of adolescent goiter, which gave the average B. M. of −9 per cent.

(To be continued)

Practical Therapeutics

Sex Gland Therapy

THE endocrine functions of the sex glands are becoming increasingly better understood. In the case of the female sex hormones remarkable additions have been made within the past few years. Potent preparations of both follicular and luteal hormones have been produced and their relation to each other and to the sex hormone of the anterior pituitary in menstruation and pregnancy are beginning to be understood. Likewise in the case of the testicular hormone there has been produced by several groups of research workers active potent and concentrated extracts exerting remarkable biologic effects. The experimental work has demon-

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strated beyond all question the presence of these active sex hormones, both male and female. They may be extracted and produce constant effects. In the case of the ovarian follicular hormone, it has been prepared in crystalline form and shows a potency that is truly astonishing. Both male and female hormones may be given hypodermically or by mouth, and the literature contains sufficient evidence of the clinical value to warrant a much wider use. Novak has outlined a method of treatment using both ovarian hormones that is in accord with the recent research showing the interaction of the follicular and luteal hormone. Whole ovarian substance would now appear to be more promising as a therapeutic agent than purified preparations of either follicular or luteal hormone. Hofbauer (abstract below) outlines the uses of whole ovarian substance. It is worthy of note that Hofbauer, as Graves of Boston has done, emphasizes the use in the menopause. This seems to be a field in which whole ovarian substance is particularly effective. Note Hofbauer states that the preparation should be used "when it contains all the active constituents of the ovary."

The Action of the Sex Gland Hormone on Total Metabolism. — R. Hofbauer. (*Zeitschr. ärztl. Fortb.*, 25: 110, 1928.)

The indications for the use of whole ovarian substance when it contains all the active constituents are:

(1) The treatment of complaints of the menopause. A disappearance of all symptoms is observed: palpitation of the heart, perspiration, dizziness. The women again become vigorous and able to work. The effect of ovarian substance is partly an inhibiting one on the sympathetic.

(2) Treatment of obesity as it may exist in the menopause as well as in young women with lowered sex gland function. Through intensive use of ovarian substance with any diet, a considerable loss in weight may be attained in many cases.

(3) Treatment of Basedow's disease. Here, the lipoid content of the ovary probably acts in so far as it appeases the two strongly acting thyroid hormone and in some measure detoxicates.

(4) Genuine epilepsy, which is of angiospastic nature, is also considerably improved by sex gland preparations.

Therapeutically, tablets as well as injections are recommended.

The authors carried on experiments to determine whether the metabolism and blood pressure are to be influenced by sex gland hormones. He made the observation that all patients felt unusually well following treatment with sex gland extracts. With a food intake of 1700 to 1800 calories daily weight decreases of 12 to 14 pounds were attained on the average within 9 weeks, without any disturbances whatever of the general state of health appearing. In men, the loss of weight in 10 weeks was on the average about 20 pounds, while appetite generally increased. In men as well as in women, a definite fall in blood pressure was obtained. In all probability an antagonism between suprarenals and sex glands plays a rôle here. In any case, a fall in blood pressure of 20 to 30 mm. may be obtained.

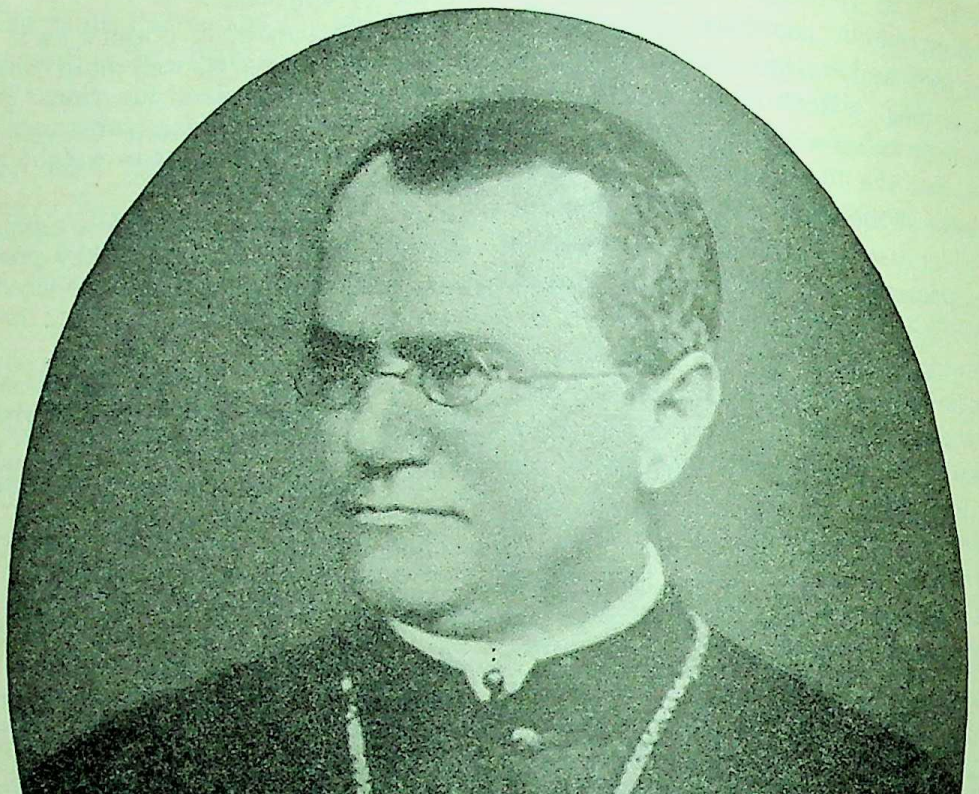
THE FAMILY PHYSICIAN

"It has been my good fortune to have intimate knowledge of physicians from childhood—personalities who went by the old and fortunate name of the family physician, the man who was elder brother and counsellor, who was almost as much nurse as doctor, who cared mightily for every patient, who stopped at nothing, whose tenderness matched his skill, and whose devotion went parallel with his service. To have those contacts, to have those memories, to have those relationships is itself a liberal education. That is why I prefer, speaking as a layman and for the patient, to dwell not on the technical aspects of medicine, not any of the new scientific discoveries and methods and possibilities, but upon that larger view which sees the modern physician as the trained man of science and public service, rich in personality, serene and secure in the feeling that others depend upon him, and holding himself for one of the highest and most satisfying services to his kind. The very verb 'to heal' sounds like a benediction."—Nicholas Murray Butler, in Clinical Excerpts.

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The Doctor's Page



GREGOR JOHANN MENDEL

(1822-1884)

Monastery walls have been quite effective not only in secluding the inmates from the whirl of the outside world but also in excluding the prying interest of outsiders as to what is being done within the confines. How much these walls have withheld concerning the life and work of the Augustinian monk and abbot, Gregor Johann Mendel, and how much they are responsible for the concealment of the results of his researches until the re-

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discovery almost twenty years after his death can not be determined definitely. Some service they did render him, however, namely made possible the success of his experimentation and afforded him a position of distinction to augment the value of his work.

Not much is known of Mendel as a man for his intimate letters to the family were few. Women, to whom he might have confided his secret thoughts and ideals were automatically barred by his choice of life. Letters to friends and fellow-workers were all mainly concerned with the work in which he was intensely interested. The letters of the closing years of his life, particularly to his nephews of whom he was very fond, are those of a kindly, peaceful, fatherly advocate; they are attractive bits of composition especially for the wit which formed an element in Mendel's make-up. A short autobiography gives little more than his letters. However, to a resident of Brünn, Hugo Iltis, we are indebted for a splendid accumulation of facts concerning the life and work of Mendel.

Johann Mendel was born in Heinzendorf, in northeastern Moravia, near the union of the German, Polish and Czechoslovakian borders, into a peasant family. From his father he acquired an intense appreciation for the growing things of the earth. His mother instilled in him an aim to a higher social standing. From her he seems to have derived a fine artistic sense. At her instigation he was sent to the gymnasium at Troppau where he showed himself to be a fine student. The cost of enlightenment, however, eventually drained the family resources, and since there were other children in the family to be considered, Mendel was left to seek his own support. His greatest desire was education and therefore, in 1841 he entered the college at Olmnetz; but the efforts expended in acquiring sufficient funds for the undertaking began to exact their toll with the result that Mendel's studies were continually interrupted by breakdowns. After two such years of intermittent study and illness he decided to enter the Augustinian order and as a novice he was given the name Gregor.

He was particularly fortunate in the choice of abbey, for the abbot of Brünn recognized his bent for natural science and encouraged his scientific work and liberal ideas rather than cared for his soul, though, as a result of a series of *faux pas* and too liberal expression Gregor was properly chastised, specifically for having remarked that a "visiting bishop was more distinguished by his fat than by his learning."

Gregor was assigned to assist in the instruction of physics at the Technical High School. His tranquil nature and sly wit made him popular so that eventually the abbot sent him to Vienna to try for a Teacher's Certificate. Gregor failed the examination, it is said mainly because of the antagonism of the board of examiners. The abbot, of course, was displeased, but his faith did not waver. He sent Gregor to the University at Vienna for further preparation. Here the monk seemed to fare well and with the exception of having purchased, so he says, a lottery ticket, he apparently devoted himself solely and diligently to the pursuit of studies. Some time later he again essayed the examination for the certificate, but rumor has it that he returned to Brünn with head wrapped in bandages, a hazy recollection of having been in Vienna, but no teacher's certificate. In fact, he never obtained it.

At the convent Mendel spent much time in the laboratory in which he kept birds, mice, a fox, and a porcupine. In the garden he kept bees, grew flowers and shrubs in profusion and in a hot house, such unusual fruit as the pineapple. These growing things he referred to as his children, indeed he cared for and nourished them beyond imagination. Besides his experiments and instructive occupation, reading occupied much of Mendel's time. Darwin's books, of course, were forbidden to good catholics, but this free-thinker, in some way, managed to procure them and read them with profound consideration. He was also attracted to the study of astrology and for years, even up to the close of his life, he kept a meteorological record.

In 1868 Mendel was elected abbot of Brünn. He then gave full sway to his experimental bent. Things grew in profusion all over the laboratory. The garden was greatly increased and became a veritable paradise of sweet-smelling and rare blooms. He also indulged in a life of ease and good eating, entertaining guests much after the fashion of the abbots of former days, for he was a lavish host.

The experiments of this unusual cleric scientist were always shrouded in mystery, which was the source of comment and discontent among both associate monks and laity. As time went on there occurred several

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Medical Subjects by Famous Masters



"A BARBER SURGEON REMOVING A PLASTER FROM A MAN'S FOOT," by David Teniers (1610-1690)
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Editorial Comment

The Journal of Organotherapy

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This Journal is issued in the hope and with the belief that it will be a source of useful information to the medical profession. It is our aim to present each new finding or important development in the field of organotherapy the moment it is brought to light. Our readers can help to make this publication of ever-increasing value to themselves by advising us of their results with organotherapy. We shall be pleased to receive such reports, and shall gladly publish them in the JOURNAL whenever our space requirements permit.

Pituitary Extract and Its Influence on the Intestine

THE use of pituitary solution in acute atony of the stomach is described by Königsberger and Mansbacher (abstract below). With injection of 0.5 to 1 cc. they essen the period of chyme retention in the tonic stomach. This effect is lacking in the tomach with normal tonus.

The earlier reports of the action of post-ituitary solution on the intestine agreed as o its stimulating influence resulting in definite contraction. Thus, injection into abbits induced defecation and strong per-staltic movements. Intestinal strips bathed n a solution of post pituitary showed con-raction and it was believed that the post-ituitary principles exerted a direct effect on e unstriped muscle.

Subsequent research on the subject, how-er, resulted in some apparent contradic-ons of the conclusion on which the earlier vestigations had been practically unani-mous. Under some conditions decreased tonus and lessened contraction were reported. The pre-existing conditions of tonus and the preliminary action of certain drugs seemed to modify the result. Other investigators reported a preliminary decrease in tonus followed by a decided increase of tonus and peristaltic movements. Some observers have demonstrated quite opposed effects of strong or weak solutions, and a marked dependence on the degree of tonus present in the muscle at the time. The effect of post-pituitary solution also seems to vary in different parts of the alimentary tract. In Königsberger and Mansbacher's article a report is made of stimulation of tonus and contraction in an *atonic* stomach. This seems to be consonant with recent work showing the dependence of the effect of existing tonus. X-ray studies of the effect of post pituitary on the stomach have also shown a primary depressing influence upon peristaltic movement and motility followed by an increase in both.

The clinical use of post-pituitary solutions in ileus, intestinal paralysis, atony, etc. needs further study before it becomes the effective agent that its action suggests.

Therapeutic Investigations with Pituitary in Atony of the Stomach in Nurslings and Young Children. — E. Königsberger and W. Mansbacher. (*Zeitschr. Kinderheilk.*, 44 : 1929.)

In acute atony of the stomach an abbreviation of the length of retention of chyme in the stomach may be obtained with an injection of 0.5 to 1 cc. of hypophysin. In normal tonus of the stomach this effect is lacking. By means of a combination with 0.0003 gm. atropin or the less reliable adrenalin (0.0003) the hypophysin effect is intensified. Clinically, after administration of the combination in severe acute atony of the stomach an abrupt cessation of vomiting was to be observed. The former hunger cure, which was undertaken for the evacuation of the stomach is hence superfluous.

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Abstracts

Malignancy of the Thyroid. — Norris W. Gillette. (*Am. J. Surg.*, **2** : 556, June, 1927.)

Carcinoma occurs in about 3 per cent of all cases of thyroid resections. Patients have a good chance of recovery if the diagnosis of malignancy is made by the pathologist and not by the surgeon, *i. e.* postoperatively. Metastases of the thyroid are of thyroid type cells developing thyrotoxicosis.

A nodular gland is surgical and early removal will save many from death from carcinoma. Extension is early by way of the blood vessels, later direct and by lymphatics. There is no such thing as benign metastases of thyroid gland.

Insulin Edema. — I. M. Rabinowitch. (*Canad. Med. Assn. J.*, **17** : 685, June, 1927.)

Insulin produces an edema of the body tissues of the diabetic person, and this largely accounts, in a great number of cases, for the rapid increases of body weight so frequently noted. The recognition of this phenomenon is important in order to estimate properly the progress in a case of severe diabetes. The proof that the rapid gains of body weight are due to a large extent to water retention is the fact that, as the insulin is discontinued, polyuria occurs, and approximately parallels the loss of body weight. Hyperglycemia gradually increases during the first few days after the insulin is discontinued but glycosuria is frequently absent. The polyuria thus differs from that of active diabetes. Obviously, if the insulin is discontinued for a certain period, the diabetes becomes active, and glycosuria reappears. Following institution of insulin treatment, without alteration of food or fluid intake, the polyuria disappears, and the patients again begin to gain weight. Rabinowitch reports two cases as typical illustrations of this phenomenon.

Insulin edema may, at times, be harmful, in view of Joslin's suggestion that it may be a factor in the production of the anuria which develops during coma. It is interesting to note that just as a suggestive relationship between insulin dosage and edema is found, so Joslin finds such a relationship between insulin dosage and anuria.

Encephalitis Lethargica. — George Riddoch. (*Brit. Med. J.*, No. 3481 : 537, Sept. 24, 1927.)

Encephalitis lethargica is essentially a chronic disease. One never knows when the patient is cured. In the late stages of the disease endocrine disorders are frequently met with. Adiposity, with or without disturbance of the sexual functions, is by no means uncommon. Duncan found it in 7 out of 83 cases. One of the author's patients, a young girl, who became rapidly and grossly fat after an acute attack of the disease, had amenorrhea lasting for many months. Later she developed exophthalmic goiter, and her weight diminished, but did not fall to normal until she made an apparently complete recovery in 18 months. In another case tachycardia, tremor, slight goiter, and emotional instability appeared in a girl a few weeks after she had seemed to recover from the acute phase of her illness, and persisted for many months. Diabetes insipidus and glycosuria are also occasional late results of the disease.

Ovarian Hormone in a Water-Soluble Form. — F. Dickens, E. C. Dodds, and D. J. Trescott Brinkworth. (*Lancet*, **212** : 1015, May 14, 1927.)

A method is described for obtaining the estrus-producing hormone in a water-soluble form by extraction from placenta, the yield being over 1000 rat units per kg. The activity of the preparation can be easily reduced to below 0.5 mg. per rat unit. Further work indicates that this degree of purity may be exceeded without much difficulty.

The product obtained is a pure white powder very soluble in water. It can be boiled in aqueous solution for a considerable period without loss of activity. The active principle passes completely through a collodion mem-

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brane, and the substance may be purified to some extent by this means. The chemical constitution is being investigated. The substance appears to be relatively simple and contains a fairly large proportion of sulphur. The Pauly reaction for histidine is strongly positive. Tryptophane also appears to be present.

Thyrotoxicosis and Associated Vagotonic and Sympathicotonic Syndromes.—Virgil E. Simpson. (*Am. J. Surg.*, **3** : 249, Sept., 1927.)

Since the symptomatology of a toxic thyroid is so closely linked to the sympathetic nervous system it would appear that the line of cleavage between vagotonia and sympathicotonia drawn by Eppinger and Hess would have an intensely practical value. Lack of uniformity, however, in designation of these two divisions of the autonomic system has added to a confusion already existing based on an anatomical separation difficulty. Langley's pronouncement is, probably, as workable as any other. According to him the autonomic system embraces the entire sympathetic nervous system and is divided into: (*a*) The sympathetic autonomic, including certain fibers of the vagus nerve. (*b*) The vagal autonomic. Under the first grouping are placed all the nerves that pass through the ganglionated cord, and in the second, the remaining vegetative fibers or expanded vagus. The ganglionated cord referred to, also called the trunk, passes parallel to, and in front of, the vertebral column and presents a corresponding ganglion for each vertebral segment. The autonomic system is also called the vegetative nervous system and may be visualized as an outgrowth of the cerebrospinal system. This nomenclature would seem simple and sufficient, but the perplexity lies in a manifest lack of agreement in designating the same thing by the same name.

The vegetative system may be divided anatomically into two units. One is composed of fibers originating in the middle portion of the thoracic and the upper lumbar cord which pass through the ganglionated cord after which many become mixed with other fibers and their identification where they terminate as end organs becomes difficult or impossible. The fibers of the other unit have their origin in the brain, the medulla

(*Continued on page 284*)

A Gynecologist's Opinion

"Functional amenorrhoea—the amenorrhoea or oligomenorrhoea that is seen in fully developed women, who have previously menstruated normally, is accounted for as a result of functional ovarian deficiency, a theory that finds strong confirmation in the almost immediate beneficial effect which ovarian extract usually has on these cases." (*Gynecology*---Graves)

The ovarian deficiency may be due to deficiency of the anterior pituitary the "motor of the ovary." Prescribe

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and the sacral segment of the cord and do not have a relation to the ganglionated cord.

The physiological facts are more uniformly agreed upon. The vegetative organs have a dual nerve supply which is antagonistic. This double innervation of these organs not under the control of the will is of tremendous importance, and this mutually antagonistic arrangement maintains a balance in function which is indispensably protective. However, the physiological process though it appears simple is influenced by the endocrines. The secretions of these glands exert a powerful effect on the mechanism of body metabolism. The action, so far as known, of the endocrine secretions on metabolism would seem to justify grouping them into those (*a*) activating, and those (*b*) inhibiting it. In the first group may be placed the thyroid, suprarenal and pituitary glands while in the second group would be found the thymus, pancreas and parathyroid glands. This relationship to metabolism covers proteins, fats, carbohydrates and mineral substances. Whenever the balance between the sympathetic and vagal autonomic divisions which exists normally is disturbed one or the other obtains the ascendency. Certain of the endocrine hormones act through the vagal division alone while others act through the sympathetic and yet others act through both. The adrenals are active, powerful sympathicotonic agents while the pancreas exercises an equally selective effect on the vagal division. Thyroid secretion expresses itself through both, hence, the hypothyroid patient is not purely vagotonic nor is the hyperthyroid victim purely sympathicotonic.

Viewed clinically, vagotonia appears to be a chronic state of vagal excitability and the organs supplied by this system will be found to be in a state of irritability. Recalling the structures receiving their nerve supply through the vagal system, the symptoms of vagotonia become a matter of multiplied physiological action. Through it the gastric and pancreatic secretions are increased, peristalsis reinforced, the heart slowed, Zinn's zone relaxed and the pupil contracted.

Sympathicotonia is practically a normal condition in females and though occurring in a fairly large percentage of males it should be looked upon in men as a stigma of feminism. Its anatomical as well as physiological anomalies occur chiefly in the nervous cardiovascular system. Neuropaths and psychopaths are common in this group, likewise neurasthenia finds plentiful recruits in these unstable nervous individuals. The author gives a grouping of the symptoms of vagotonia and also of sympathicotonia. Charts showing vagal and sympathetic predominance in thyrotoxicosis are also given.

While the manifestations attributable to either the vagotonic or sympathicotonic group may be kept in mind, yet they will be disconnected.

Acromegaly. — Harvey Cushing. (*Brit. Med. J.*, No. 3470 : 48, July 9, 1927.)

The surgeon before operating in cases of acromegaly must seriously take into consideration the influencing by operation of the secondary effects of hyperpituitarism. Serious consequences ensue upon damage to the hypothalamic center. It is a region to be shunned lest diabetes insipidus, excessive adiposity, and even a fatal cachexia supervene. Evans and Smith by their work have shown that the hypophysis is primarily concerned with growth. No less definitely do their experiments show that it is an activator of the reproductive organs. Nature has provided that neither the pathological giant nor dwarf should reproduce his kind. These states, which necessarily originate in preadolescence, are represented by corresponding ones which set in later in life when normal skeletal growth has been attained. In these circumstances, too, for different causes apparently in the counterposed states of hypophyseal overaction and underaction, the functions essential to reproduction are interfered with. But this is only the beginning of a long sequence of alterations in other glands, affecting the thyroid and pancreatic islets in ways but partly understood, the parathyroids, adrenal cortex, and the rest in ways not understood. Then there are the final stages in the two conditions of glandular insufficiency and overactivity; on the one hand the tissue atrophy with resultant senility and cachexia; on the other hand, splanchnomegaly and tissue hypertrophies are produced which, as in the case of the heart, lead to equally dire consequences. Not until some practical form of substitution therapy is at the surgeon's call will he properly run the risk of overdoing his extirpation, for a daily homoplastic transplant so strikingly effective in the hypopituitary rat is out of his reach.

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The Pancreas Hormone of the Unborn Child. — Holzbach. (*Zentr. Gynäkol.*, **53** : 1907, 1929.)

Examples of the presence of fetal insulin are presented from

1. The anatomical structure: the incretion-producing island apparatus in the newborn is about four times more powerful than in the adult. In the embryo it is developed much earlier than the excretory parenchym.

2. The physiological confirmation of the activity of fetal island apparatus producing the incretion is brought out by the fact that the ferment-free pancreas of ox fetus was given as an insulin restorative. By means of refinement of method (mouse test) the active incretion is also to be observed in the human fetus. The author has found it in human fetuses of all ages, beginning with a fetus 21½ gm. in weight. In dry weight, *i. e.* derived from 1 gm. of pancreas, the fetal pancreas exceeds the adult pancreas many times in insulin content. By means of animal test and clinical observation the fact is definitely determined that the blood of the mother passes through the placenta with a slight loss of sugar content, however, it experiences an effective exhausting of blood sugar in the fetal organism. The author presented the assumption that this exhaustion is executed by means of a pancreas incretion in the fetal body, following his observation on diabetics who were pregnant. Through the work of Laqueur it was shown that the female sex hormone is not so strongly antidiabetic that it can depress the heightened blood sugar content of pregnant diabetics to normal.

On the Question of Endocrine-Toxic Epilepsy (Serejski). — E. N. Krylowa. (*Zeitschr. ges. Neurol. u. Psychol.*, **121** : 521, 1929.)

The importance of the endocrine organs for the pathology of epilepsy according to Redlich, are shown to be most convincing if it is possible, by means of an arrangement of one or more organ preparations, to obtain a specific therapeutic effect in epilepsy. The author studied three cases of epilepsy under endocrine treatment, in two cases hyperthyrosis and in one case ovarian insufficiency were demonstrated.

In both of the former cases the Lugol treatment and in the third patient the administration of ovarian preparations led to extensive improvement and a reinstitution of the working capacity. In the determination of the syndrome of endocrine-toxic epilepsy the author sees a new means of prognosis and therapy of a certain number of cases which were previously held to be hopeless.

Uterine Movements and Maturation of the Ovum. — Kok and Seel. (*Klin. Wochenschr.*, 8 : 1265, 1929.)

The normal physiological movements of the uterus in the animal are stronger at the time of estrus than in the inter-estrus, in the tubes the opposite was found. Adrenalin makes it possible for these movements to increase. In the uterus of the hog there is no synchronism, the change occurs more in the topographical-anatomical course, from within out.

On the Physiology of Corpus Luteum. — Hermann Knaus. (*Arch. Gynäkol.*, **138** : 201, 1929.)

As the investigation of the author shows, the corpus luteum of rabbits suppresses, in hormonal manner, the maturation of follicles and ovulation. The opinion held by many sides that the corpus luteum, the ovary and the placenta form a unit is incorrect. Only a common property occurs in these three different substances, namely to call forth estrous symptoms in the castrated mouse.

Concerning the Relationship between Sexual Hormone and Hormone of the Anterior Lobe of the Pituitary and Lipoid Tolerance in Human Beings. — Carl Kaufmann. (*Zentr. Gynäkol.*, **53** : 1904, 1929.)

Investigations on thirty-seven women concerning the action of the ovarian hormone and the hormone of the anterior lobe of the pituitary on the amounts of cholesterin in the blood gave the following: During the course of a treatment by injection and also after per oral administration of large doses of the sex hormone "folliculin" a rise of cholesterin in the blood is demonstrable, which abates again with cessation of administration of the hormone. In contrast to the investigations of Reiss and Langendorf it was impossible for the author to obtain in human beings by means of injection of the hormone of the anterior lobe of the pituitary a lasting increase of cholesterin in the blood, such as occurs after treatment with ovarian hormone. Also,

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after per oral administration in doses up to 6800 rat units given to one patient, permanent rise in cholesterin remained indiscernible. Rather, in a large majority of women a characteristic change of blood cholesterin content was observable shortly after the injection. The effect of the ovarian hormone on the cholesterin content appears to be a specific hormone effect, while the action of the hormone of the anterior lobe of the pituitary as a stimulating effect must not be excluded entirely.

Therapeutic Investigations with a Certain Fraction of the Posterior Lobe of the Pituitary in Diabetes Insipidus Including Observations on Its Mechanism of Action. — S. Isaac and R. Siegel. (*Klin. Wochenschr.*, 8 : 1700, 1929.)

E. Frank, the discoverer of the relationship between disturbances of the pituitary and diabetes insipidus, has recently sought to substantiate the pituitary theory of this disease against the theory of other research workers who agree that the pituitary plays a part in the pathogenesis of diabetes insipidus and assume a localized nerve center for the water diuresis in the tuber cinereum, injury to which would result in excess excretion of urine. With regard to the value of previous experimental material which has been gathered for the support of this point of view a report is made in the contribution of Frank. Here it suffices to say that since the fact was discovered by R. v. D. Velden, of a curative effect of injections of extract of the posterior lobe of the pituitary in diabetes insipidus, numerous bits of information for a hormonal regulation of the kidney function by means of the pituitary have been brought out. Quite in this sense, also, P. Trendelenburg has recently worked on the investigation. He found that after extirpation of the pituitary there was a substance in the tuber cinereum which had the same effect as the extract of the posterior lobe for inhibiting diuresis and excretion of salt. It is present only in small quantities in the tuber cinereum of normal animals. When the urine-inhibiting substance first arises after extirpation of the posterior lobe, a vicarious formation of hormone occurs in the tuber cinereum. This finding explains all the contradictory reports of experimental research up to the present time and is a strong support for the hormone theory.

Most of the pituitary preparations used for a long time passed, such as hypophysin, pituglandol and pituitrin, are extracts of the posterior lobe which have a known effect on the smooth musculature of the uterus, the liver and the blood vessels as well as a restricting action on diuresis. Many failures in the therapy of diabetes insipidus are perhaps to be traced back to the fact that the dose offsetting the disturbance of water and salt metabolism is not sufficient to bring about the strong action on the uterus or liver musculature and hence the administration of the amount adequate for diuresis inhibition in the course of time is incapable.

Previously Oliver Kamm and his colleague worked on the problem. It was possible for him to isolate two different substances from the posterior lobe of the pituitary: the first worked only on the uterus and the second tonicized the blood vessels and intestinal musculature and inhibited the diuresis, particularly the pathological.

In the following the authors reported likewise on two special fractionated preparations derived from the posterior lobe of the pituitary. The one has, besides the effect on the blood pressure and on the musculature of the intestine, a strong diuresis-inhibiting effect which could be determined; the other acts only on the uterus musculature.

From the investigations of the authors it was shown that in hypochloremic diabetes insipidus the pressor hormone restrains the excretion of water, causes the thirst to disappear and increases the concentration capacity of the kidney for salt. Further, the reduced salt content of the blood is restored to normal. Hence, the genuine diabetes insipidus was a hormonal disease, while in the hyperchloremic cases, associated with disturbance of tissues, a central neurogeneous component was to be acceded. It is comprehensible that an intense over-supply of pituitary hormone also makes possible the remedy of the tissue disturbance; hence the water and salt metabolism ostensibly very important for the determination of the life processes is doubly assured, *i. e.*, it is regulated hormonally as well as by the nervous system.

Considered impartially, in the organism, the facilitated mobilization of salt out of the tissues and the increased capacity of the kidney for excretion of the latter, by which this takes effect with the least possible loss of water for the body, appears the essential one

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of the combined effects of the hormone of the posterior lobe of the pituitary. (Dissociation of water and salt diuresis.)

Contribution to the Study of Icterus Catarrhalis and the Treatment of It. — J. Pavel, C. Bratesco and G. Negresco. (*Arch. mal. appar. digest. et mal. nutrit.*, **19** : 696, 1929.)

The author has given insulin for the treatment of hepatitis patients. Although the insulin treatment of this disease form has been revived repeatedly, the majority of the clinicians have attributed it to various causes. Besides the insulin the author gave simultaneously sugar perorally or glucose rectally. In spite of the good effects of insulin the author, however, saw disagreeable attacks.

Concerning the Modern Medical Therapy of Diseases of the Bile Duct. — Ferdinand Lebermann. (*Med. Welt*, **3** : 1077, 1929.)

The most modern procedure for therapy of diseases of the liver and bile is treatment with sugar and simultaneous administration of insulin. It should incur the retention of glucoses in the liver and hence forestall the imminent injuries due to glucose impoverization. Very good results have been reported by many authors with this insulin-sugar cure in accordance with the procedure of P. F. Richter and Umber.

Biology and Clinic of Sleep. — Poetzl. (*Jahreskurse ärztl. Fortb.*, **20** : 6, 1929.)

Cushing and Goetsch have demonstrated involution symptoms of the pituitary in the winter sleep in animals and refer this condition to changes in pituitary secretion (anterior lobe). Adler was able to determine experimentally that the hedgehog in winter sleep, could be awakened by a subcutaneous injection of thyroid gland extract. This confirms the hormone dependency of winter sleep. Thymus extract, adrenalin and anterior lobe of the pituitary have the same effect. Adler describes the winter sleep as a result of hypofunction of the thyroid, evidently also of the pituitary and suprarenals.

Salmon has presented a hormonal hypothesis for normal sleep. The detoxication of the toxin of fatigue proceeds through the activity of the endocrine glands. When these function poorly, eventually sleeplessness occurs. According to Mingazzini and Barbara the hormones of the thyroid, the suprarenals, the genitals and the hypophysis exercise a promoting action during the waking hours. In sleep, however, "the hormone acting anabolically on the tonus of the autonomic system" would come into effect.

Genital Hemorrhages in Young Girls. — F. Kermauner. (*Arztl. Praxis*, **3** : 235, 1929.)

One is inclined today to assume a disturbance in the coordination of the incretion organs in rather obscure cases. There are many examples known of this. There are girls with intense hypothyroidism and genital hemorrhages. Administration of thyroid gland sets this in order in a short time. Besides the older remedies the author is inclined to give pituitary preparations as coagulant medium. Likewise in pronounced hypoplasia ovarian preparations, but only the best and most active and only for a short time.

Contribution to Thyroxin Treatment of Congenital Myxedema. — Nobel and Kornfeld. (*Zeitschr. Kinderheilk.*, **48** : 216, 1929.)

The authors report on a 17 year old girl previously untreated, with severe congenital myxedema, in whom after 1½ years of continuous thyroxin treatment an increase of body growth up to 18 cm. and a quite complete reconciliation of the former high degree of retarded ossification could be obtained. The changes in the soft parts to effect the reconstruction are particularly rapid, while the mental development in less satisfactory manner derives from the thyroxin treatment only what is to be expected from an all too long life period without treatment, in exhausted athyrotic state.

Endocrine Pancreas Therapy in Chronic Venous Disturbances and Their Complications. — Pierre Quiserne. (*Paris med.*, **19** : 156, 1929.)

The treatment of varicose ulcers by means of local insulin application in the form of salve or ointment, gives quite varied results. In one case prompt cicatrization of the varicose ulcers was obtained, in other cases the treatment remained ineffective.

The author treated experimentally with insulin injection patients who suffered from Claudicatio intermittens, and obtained satis-

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factory results therewith. The influence on the trophic disturbances of the skin obtained by this method of treatment was striking. This observation led to the investigation of peroral dosage of total substance of the pancreas gland. This method of treatment far surpassed the insulin injection method, as well regarding spasmodic vasomotor disturbance of the Claudication as the trophic disturbances of the skin and other tissues. This last was corroborated by use of peroral gland administration in patients with varicose ulcers. The skin lost its infiltrated appearance, was again supple and acquired also an approximately normal color. Even the pigmentation in several cases showed a definite involution. There is no doubt that pancreas treatment in these cases had good results; also it seems that the administration of other endocrine gland substances along with the pancreas, augment the effect of the latter or activate it. In this sense, indeed, the parathyroid substance is to be regarded as an adjuvant. The same holds true in the internal application of ovarian and testicular substances in varicose ulcers. The pancreas substance itself, through its anti-spasmodic effect, on the vasomotor, seems to have a favorable influence on the painfulness of this form of disease.

Studies on the Cardiovascular Effects of Insulin. — Carl-Eric Räihä. (*Skandinav. Arch. Physiol.*, **57** : 243, 1929.)

From the author's experiments it was shown that:

1. After intravenous injection of insulin the volume per minute of the heart is decreased. The slight degree of decrease lasted for a time.
2. After an intravenous injection of insulin the blood pressure in the aorta falls for a time (about 10 to 30 minutes).
3. Directly following an insulin injection the blood pressure in the Art. pulmonalis is raised; later a depression of the pulmonalis pressure occurs which, in most cases, again passes to a blood pressure increase.
4. After an insulin injection the vagus-stimulating effect on the heart decreases to a greater or less degree. This decrease of effect of vagus stimulation as a rule was raised for a time after the administration of a subsequent adrenalin injection. During the increased pressure state caused by adrenalin the effect on the heart of the vagus stimulation is greatly offset.

The Physician's Interest Is a Human Interest

The primary concern of the physician lies in the welfare of the patient. The laboratory and research workers have special problems and phases of a disease process uppermost in their mind.

The physician in practice is treating a patient and he is attempting to restore the health and well being rather than to influence particular phases of the disease affecting his patient.

It is possible to favorably influence the entire diabetic process; increase the strength of the patient; favor the regeneration of the defective pancreas; modify the disturbed carbohydrate metabolism.

These effects are possible with Trypsogen which contains not a single pancreatic hormone affecting a single phase of diabetes, but a number of internal pancreatic secretions necessary (as shown by experiment) for maintenance of normal health and the enzymes which are lacking in diabetes.

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Therapeutic Investigations with Liver in Schizophrenic Diseases. — Eugen Rakonitz. (*Monatsschr. Psychiat. u. Neurol.*, **73** : 116, 1929.)

An under-cooked preparation was administered, which had been given in pernicious anemia with successful consequences. The preparation had the drawback of not being injectible and hence incited aversion as does every intense feeding of liver after a time.

The duration of feeding was 30 to 50 days. Five paranoids, seven cases of dementia simplex, five hebephrenes, two catatoniacs and three stuporeses were treated. The body weight of the patient increased in twelve cases during treatment. The formation of blood showed a tendency to recover in seven anemics. Digestive disorders were not released through the treatment. In those patients with depressed spirits the temperament was improved. In many cases the general condition was improved. There was no observation to portend the fact that liver treatment, as substitution therapy has any specific effect. With the preparations used, the behavior was similar to that with hormone preparations in general. It is not known what they contain. However, substitution therapy remains for the time being, the only conceivable method of investigation.

Clinic and Therapy of Hemorrhages in Puberty. — H. Runge. (*Zentr. Gynäkol.*, 53 : 2252, 1929.)

Curtailing operations and castration must be avoided in all cases. In isolated cases improvement ensued after injection of pituitary extract and suprarenin, other cases reacted well to insulin. However, it is possible only in a few cases to avoid relapse from the beginning. Treatments with ovarian hormone preparations are contraindicated in glandular cystic hyperplasia of the mucous membrane of adolescents, since the investigations at the Kiel Clinic have shown that the hormone status in glandular cystic hyperplasia is raised above normal.

On the Liver Therapy of Pernicious Anemia. Continued Observations on Twenty-Five Perniciosa Patients Treated with Liver. — Hans Schulten. (*Münch. med. Wochenschr.*, **76** : 1281, 1929.)

Twenty-five patients were observed continuously for 2 to 3 years. Liver therapy is not only the best medium against blood changes of perniciosa, but it is also, mainly, the most secure method of treatment, and it is a mistake not to give it. In the medical polyclinic of Hamburg University (resident division) liver extract in amounts of 40 to 100 cc. corresponding to 250 to 600 gm. fresh liver was given. In most cases 20 to 40 cc. were sufficient for the support of the therapy. The proposition may be offered that practically no relapse occurs with adequate liver therapy. Indeed, even with deficient or inadequate liver administration a remission may be warded off for a long time. In each case it may be said that the prospects of liver therapy for perniciosa patients have been greatly improved by means of liver therapy.

The Influence of Hormones on the Sugar Distribution and Cell Permeability in the Animal Organism. — Rudolf Siegel. (*Klin. Wochenschr.*, 8 : 1659, 1929.)

From the exhaustive investigations of the author it is shown that under physiological conditions insulin promotes sugar deposit and glycogen fixation in the liver, in the musculature it raises the infiltration capacity of sugar and raises the conversion of this into glycogen under simultaneous oxidation of an insignificant portion. In very low concentration adrenalin, under physiological circumstances, acts in the same manner as insulin, namely glycogen-fixating. In the body periphery it is its antagonist insofar as it restricts coincidently the recurrence of blood sugar in the musculature. In cases of glycogen impoverization adrenalin excites the liver by furthering the formation of lactic acid from muscle glycogen to a new formation of liver glycogen. Adrenalin is almost without effect on the oxidative sugar metabolism of carbohydrate. Only in abnormally high concentration (shock, experiment) did adrenalin act in an opposite sense, glycogen saccharification by stimulation of the sympathetic terminal in the liver. In thyroxin, however, we must perceive the real antagonist of insulin and adrenalin in the liver, while in the body periphery a direct influence on the carbohydrate metabolism under thyroxin was not to be demonstrated.

For the maintenance of normal carbohydrate metabolism the harmonious alternate play of the individual incretions is of greatest importance. The way in which disturbances of the hormone equilibrium under pathologi-

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cal conditions act, for example in diabetes mellitus, will be reported in another communication.

New Contributions to Our Hormone Studies. — Siebke. (*Klin. Wochenschr.*, **8** : 1644, 1929.)

Siebke uses the hormone prepared by him therapeutically for stimulation. The preparation was put through a Berkefeld filter in highly concentrated solution, and by means of 2‰ tricresol is preserved in ampoules. No evidences of irritation are to be found after injection. The content of the solution in mouse units is constant the month long, up to the present. Sexual hormone: Quantitative investigations (method of Laqueur) on the amount of sexual hormone in the urine of women, outside of pregnancy, gave evidence that the entire amount excreted during a cycle (from beginning of a menstruation up to the next menstruation) varies between 250-1000 to over 2000 mouse units (!). In venous blood at the most there is found from 1 unit to about 7 the third day after menstruation in 25 to 40 cc. In accordance with Laqueur's plan for every cure about 10,000 mouse units of ovarian hormone would be given in dragées. (Commencement of the cure 12 days before the expected or desired menstruation, increasing amounts, sudden cessation after maximal doses.) Good and in some cases very good results were obtained in proper indication. Corpus luteum hormone is lacking in metropathia hemorrhagica (histological glandular cystic hyperplasia). The sexual hormone, corresponding to the persistence of the follicle is demonstrable in high concentration in venous blood until well into the time of bleeding.

A Stimulation Substance of the Central Organ and the Central Function. — E. Steinach, partly collaborated by H. Kun. (*Med. Klin.*, **25** : 1221, 1929.)

On the basis of experimentation the author comes to the conclusion that the problem of incretory function of the central organ is elucidated and the experimental basis for a relative hormone investigation is given. From the brain the author derived a stimulation substance which is obtainable in large quantities from the brain cortex substance and which may be identical with the hormone of the anterior lobe of the pituitary. Doubtless there are relations or correlations between the brain stimulation substance and other incretions. Perhaps it will follow that diseased conditions of the central nervous system and psychic anomalies are based upon a lack of or a defectiveness of the stimulation substance. In all such cases therapeutic application can be assigned.

The Influence of the Endocrine Glands on the Healing of Diseases. — A. Theilhaber. (*Münch. med. Wochenschr.*, **76** : 1241, 1929.)

The author presents the suppositions that the panhormone in many diseases is more necessary than the pure hormone, the intact living substance more active than that injured or destroyed in the factory, the whole organ more necessary than the extract. An instituted tissue depot in the sick body acts better than injection repeated several times weekly, and by oral application many valuable substances are indeed destroyed by the juice of the digestive canal.

Implantation effects a powerful increase of all the living processes of the organism, in amenorrhea menstruation is often recommenced. In twenty-six patients with disorders of the central nervous system (spinal anterior poliomyelitis, multiple sclerosis, syringomyelia, encephalitis, etc.) the author has treated them with implantations of spleen, thymus, thyroid gland and liver and gained improvements in some and in one case, cure. Likewise the struggle of old age and the diseases of old age is resumed by this method. The stimulation of the hormone is a very important factor for the growth of the organ. Thus, in infancy, for example, if the hormone of the ovary is lacking the uterus is underdeveloped. If the hormone of the ovary is again decreased *post climacterium*, the uterus atrophies. The activity of the organ to be implanted is augmented by treatment of the animal from which it is taken. The administration of endocrine gland substances prophylactically in various diseases and of gland extracts in premature senility is desirable.

Influence of Pituitrin-Snuff Powder in Severe Diabetes Insipidus. — Schalscha. (*Münch. med. Wochenschr.*, **76** : 1491, 1929.)

The author reports on the therapeutic investigation, particularly bringing out the good results effected by pituitrin in endonasal application, while it proved ineffective with *per os* administration.

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Studies on the Biology of the Placenta of the Guinea Pig. — Vilardell. (*Gynécol. et obstet.*, **20** : 65, 1929.)

Extract of fresh guinea pig placenta after intraperitoneal or intracardial injection, causes a chlorosis and unimportant changes in the kidneys and liver of other guinea pigs.

The placenta autolysate after intraperitoneal or intracardial injection causes anemia perniciosa and alterations in the kidneys and liver of other guinea pigs.

Extract of fresh guinea pig placenta possesses, when injected intraperitoneally into other guinea pigs, an anti-glycosuric action.

The author believes that the placenta of the guinea pig has a hormone effect which is stimulating on the pancreas and inhibiting on the suprarenals and thyroid gland.

Concerning Temporary Hormone Sterilization of the Female Animal by Means of Feeding Insulin. — E. Vogt. (*Med. Klin.*, **25** : 1163, 1929.)

From investigations on mice it was shown that: The temporary hormone sterilization of female animals may be obtained in the same way by feeding insulin as by parenteral administration. Hence a new fact is brought out, that insulin, at least as far as its sterilizing effect is concerned, also displays this effect in resorption from the intestinal tract.

In the fact that the female sex hormone in the form of a pure preparation of folliculin, when administered *per os*, acts in animal experiments as well as clinically, and that mice can be temporarily sterilized by feeding of insulin without the occurrence of general damages, the author sees a confirmation of his previously obtained information, that the pancreas hormone, the ovarian and the placenta hormones, or the female sex hormone, are closely allied with one another and above all display themselves in this sterilization characteristic.

Concerning the Diagnosis of Pregnancy from the Urine by the Presence of the Hormone of the Anterior Lobe of the Pituitary. — E. Vogt. (*Münch. med. Wochenschr.*, **76** : 1401, 1929.)

The method of demonstrating the hormone of the anterior lobe of the pituitary in the urine of pregnant women is a method free from objection, and technically comparatively simple, for the diagnosis of early pregnancy. The author describes the working out of the new method for clinical-therapeutic investigation by implantation of anterior lobe of the pituitary from animals and through parenteral administration of a pure hormone of the anterior lobe of the pituitary, according to the practical contribution of Zondek and Biedl.

On the Diagnosis and Therapy of Disturbances of the Pituitary. — Wiele. (*Münch. med. Wochenschr.*, **76** : 1491, 1929.)

Diabetes insipidus is to be treated with extract of the posterior lobe, parenterally, primary oliguria, however, is not definitely influenced. Simmond's disease, correctly diagnosed, can be affected with substitution therapy. Disturbances of growth with pituitary symptoms likewise give good results under substitution therapy eventually combined with substances of other glands. The condition of the pituitary dwarf can be influenced best.

Concerning the Clinical Significance of the So-Called Heart Hormone Preparation. — Max Winternitz. (*Med. Klin.*, **25** : 1218, 1929.)

According to the observations in the clinic of Professor R. Schmidt it was shown that cardiac hormone extracted from the ox heart according to Haberlandt is effective in anginoid symptoms as well as in the attack, prophylactically. According to the indication of the patients treated, nitrite is incorporated for the permanence of the effect and prophylactically. The action apparently takes effect by means of dilatation of the coronary blood vessels, which is more lasting than that of nitrite. The Zuelzer and the Haberlandt preparations do not exercise these effects which the clinicians have determined to consider as heart hormone.

On the Organ-Specific Growth-Promoting Action of Homoplastic Epithelial Cell Transplantation. — H. G. Zwerg. (*Deut. Zeitschr. Chir.*, **218** : 289, 1929.)

Very often the present homoplastic parathyroid gland transplantation in human beings for combating tetany has been refused and the internal or organ therapy *per os* has been applied as the more active. However, it has been shown that this is not always the case. For, if this were so, naturally nothing

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ought to come of transplantation. Recently, an organ preparation from out of the cortex of the parathyroid glands has often been introduced into the therapy of tetany, the Collip Parathormone. The experiences here are not unified and are too few in number to permit any extensive criticism on the efficacy. The therapy may be accomplished either by the proper organotherapy, internally, by the administration of parathyroid gland preparations, or surgically, by the transplantation of epithelial cells. Besides the specific organ therapy, a non-specific also was investigated, by means of administration of thyroid gland extracts or thyroid gland transplantation. Only a few observers, however, have reported favorable results on this. On the other hand, many favorable communications concerning the effect of parathyroid tablets have been found. Yet, reports of unsuccessful results are not lacking. An absolutely certain, active method of treatment of human tetany does not exist. As the latest medium, however, the homoplastic transplantation of epithelial cells is offered.

Concerning Coma Diabeticum. — Hermann Bennhold. (*Zentr. inn. Med.*, **50** : 881, 1929.)

By means of insulin which occasions the chief harm in coma diabeticum, other severe injuries to the organism which had remained unobtrusive up to the present, were brought out, above all disturbances of the circulation. Besides camphor preparations as therapeutic measure the author administered adrenalin and likewise tested pituitary and strychnin. With the exception of the passing success with adrenalin, no other particularly certain and effective medium was found.

Secondary Effects of Insulin. — Bonem. (*Münch. med. Wochenschr.*, **76** : 1585, 1929.)

A report on a patient, female, who presented an idiosyncratic reaction to insulin, and the presentation of an analogous case from the literature. Likewise two non-diabetics showed the secondary effect of insulin in the sense of a parenteral irritant substance. The observations warrant the assumption of a substance in the insulin preparation, which causes a secondary effect in the sense of a parenteral or enteral albumin action, and under the circumstances imperils the brilliant effect of the insulin therapy as well.

General Information concerning Hormones. — Leon Asher. (*Fortschrit. Therap.*, **5** : 564, 1929.)

Besides thyroxin, adrenalin, insulin, parathyroidin, and the hormones of the pituitary and the sex organs, in his report the author also treated with the following hormones: Cortin, the so-called Automatine, the wound hormone, the regeneration hormone, cholin, cholate, etc.

With regard to the question of whether the physiological experiments offer more favorable testimony for the application of pure hormones or other organ preparations, the author comes to the conclusion that the pure hormone preparations are to be preferred. For certain hormones the "all or nothing" law is valid, for others the phase relationship, the reversal to the contrary or the physiological activity. The regulation principle of the humor, presented by the author is of great importance. The disposition of the tissues for the effect of the hormone is either endogenous or exogenous. The influence of other hormones is of first rank among the endogenous factors. To the exogenous factors belong the effects of combinations of nutrition, climate and pathological processes.

The Presence of Female Sex Hormone and Hormone of the Anterior Lobe of the Pituitary in the Blood and Urine of the Newly Born. — R. Brühl. (*Klin. Wochenschr.*, 8 : 1766, 1929.)

From the exhaustive investigations of the author the following results were derived:

1. In the urine of the newly born, without differentiation as to sex, female sex hormone may be demonstrated up to the fourth day. Likewise it is regularly present in blood from the umbilical cord and in liquor amnii. It was not found in the milk in all instances.

2. The hormone of the anterior lobe of the pituitary — Reaction I according to Aschheim and Zondek — could be demonstrated in the urine of the newly born only until the second day and only in half the cases. In the blood from the umbilical cord it is always present, but in various concentrations. In the liquor amnii of older children it was not observed and in the milk only once.

3. In animal experiments it was demonstrated that the occurrence of the secretion of the mammary glands is associated with the

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disappearance of the female sex hormone from the body.

4. Likewise it was shown most evidently in newly born children that the mammary gland secretion is to be associated with the disappearance of the female sex hormone.

Impetigo Herpetiformis in Post-Operative Tetany and Parathyreoprivic Cachexia. — Felix Danisch. (*Frankfurter Zeitschr. Path.*, 38 : 290, 1929.)

In diseases of the glands of internal secretion the relation of the vegetative nervous system has been but slightly investigated up to the present; for only a few endocrine glands, for example the adrenals, the thyroid gland and pancreas is the "closed functional circle" (Asher) of both systems well known. Indeed the author brings out known, but little credited facts: Each alteration in functional condition of an endocrine gland incurs a change in the functional status of the vegetative nervous system. The correlative changes in other endocrine glands in the case of disease of one of the incretion organs is to be explained as partly humoral, *i. e.* by direct incretion effect, partly due to the accommodation of the vegetative nervous system. At any rate the direct or the correlated impairment of the function of one, under the circumstances, seems also to be reflected in the several incretory organs and by means of change in ion concentration and disturbances of calcium metabolism leads to a dysfunction of the vegetative nervous system. In all disorders of calcium metabolism, besides the loss of calcium, the shifting of the blood calcium, ionized and bound to the albumin substance, is very important. Besides epithelial material the thymus, thyroid, pituitary and the sex glands also have an influence on the calcium metabolism. In impetigo herpetiformis in males and likewise in non-gravid women one invariably finds clinical evidences which permit conclusions as to the functional disturbance of the organs mentioned.

Of What Significance Is the Determination of Basal Metabolism for the Practicing Physician. — Fritz Fleischer. (*Zeitschr. ärztl. Fortb.*, **26** : 593, 1929.).

In therapy the calculation of the basal metabolism has shown that in the case of hypofunctioning of the thyroid gland, thyroid gland preparations (thyroxin) can elevate the basal metabolism. In hyperthyrosis antithyroidin Moebius, ovarian preparations, ergotannin and röntgen as well as radium radiations lower the basal metabolism. Hypofunction of the ovary was favorably influenced by sex gland preparations. The substance of the posterior lobe of the pituitary leaves the respiratory quotient uninfluenced, but effects an increase of O_2 and CO_2. The anterior lobe substance of the hypophysis raises the respiratory quotient and offsets the O_2 and CO_2. In blood diseases thyroid gland preparations prove effective.

Concerning the Ovarian Hormone Effect on Several Skin Diseases. — Sergei Borman. (*Dermatol. Wochenschr.*, **89** : 1441, 1929.)

The etiology of a very stubborn eczema such as urticaria univers. is given. Eczema, pruritus and acne vulgaris, under the circumstances were referred to endocrine disturbances in the main. Doczy, for example, applied the Lüttge-Mertz ninhydrin reaction with ovarian extracts as test organ in several of the skin diseases. The reaction gave a positive result forty times in 120 cases of psoriasis. Pariser presented four cases of very severe urticaria which were permanently cured after 6 weeks with ovarian or testicular preparations. Likewise the communication of Pidona and other authors on the association of alopecia areata with menstrual defect give proof of the relation of hormonal activity of the ovary and skin alterations. For further clarifying the problem röntgen therapy has a particular advantage. Especially in Russia where the need for a reliable ovarian hormone preparation has at once been felt, the röntgen experiments have a particular therapeutic interest.

Stomach Function Tests following Liver Therapy in Cases of Pernicious Anemia. — Fritz Brauch. (*Fortschrit. Therap.*, **5** : 412, 1929.)

Isolated contributions have been known concerning the fact that after liver therapy in pernicious anemia the production of HCl is again instituted in the stomach. In five of the cases investigated by the author no formation of HCl occurred after histamin injection, in all cases it was a question of a histamin-resisting achylia despite previous liver therapy. Further researches showed that in no case was pepsin or pepsinogen present.

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From the observations of the author it is shown that in the indicated cases the liver therapy effects no success with reference to an influence on the achylia gastrica.

Concerning the Relation between Joint Disorders and Sex Glands in Women. — W. K. Fränkel. (*Fortschrit. Therap.*, **5** : 513, 1929.)

It is a well known fact that during the premenstruum or the menstrual period, rheumatic processes commonly recur. The most common complaints of patients in business is pain in the joints. Most all of these women with the complaint mentioned are just about to enter the menopause or are experiencing it. No doubt the termination of the mutual internal secretion function can be considered the inciting agent for the chronic knee and joint arthropathy of all these women.

Menge was able to demonstrate that the chronic joint disease had a direct relation to the function of the ovary. He mentioned the disease arthropathia ovaripriva. The institution of a therapy with ovarian preparations, however, first brought disillusionment; nevertheless the failure of the result did not lie in the theoretical premise which led to the test with ovarian therapy, but rather in the inadequacy of the preparation administered. Since new preparations now contain standardized ovarian contents, the great need of the therapy for chronic arthropathy may be fulfilled.

In endogenous obesity and arthropathia Zimmer reached the conclusion that thyroid gland therapy effects extensive improvement in joint diseases, even before obtaining a decrease in weight.

In any case, in the disease mentioned, the question is not only one of ovarian, but also an etiologically important influence on the part of the thyroid gland. The author formerly demonstrated on this matter that the predominance of varices in women and the usual occurrence of varices in pregnancy permits the conclusion of an ovarian endocrine component.

The author derived encouraging results with doses of thyroidin. Joint pains during puberty without infection, are often found in existing hyperthyrosis. Besides ovarian insufficiency and the symptom of hyperthyrosis, participation of the adrenals can also usually be demonstrated. A pluriglandular process is evident in this disease.

A Symptom Complex in a Patient on Insulin Dosage. A Contribution to the Theory of Hypoglycemia. — Yairo Hattori. (*Münch. med. Wochenschr.*, **76** : 1634, 1929.)

As is known, sugar is used with insulin injection to forestall the outbreak of a hypoglycemic symptom complex. However, the author observed almost without exception, in the treatment of diabetic patients, a nervous symptom complex: Lassitude, a feeling of faintness in severe cases, even if there were only a transient comatose condition. When grape sugar was used the symptom complex occurred stronger than with levulose. This indication is dependent upon the amount of insulin injected and can be present without the accompanying hypoglycemia. After repeated injections of the same dose of insulin the symptom gradually fell away and in the end disappeared. One must assume an indication of poisoning and perhaps there is a substance such as, for example, glucosone, in the process of intermediary sugar metabolism. An analogy is to be found in the administration of thyroid gland substance, in which a group of symptoms such as tachycardia, tremor, high blood pressure, etc., can be brought out by thyroglobulin as well as other symptoms of increased metabolism, diuresis, etc., may be brought out by means of thyroxin.

Observations on the Therapy of Senium Praecox. — L. Heumann. (*Fortschrit. Therap.*, **5** : 454, 1929.)

The main condition of senium præcox is hypofunction of the sex glands and of the pituitary lobe. The symptoms of underfunctioning of incretory glands are naturally much less pronounced in the prematurely aged than in hypogenitalism or in castration. In the treatment of senium præcox, to which symptoms alveolar pyorrhea belongs, along with the administration of active incretions, primarily, psychologic agents are standard. Just recently the investigations of Zondek and Aschheim have again revived the discussion of the efficacy of sex gland extracts. The fact is that many of the preparations long known in test experiments according to Allen and Doisy, have shown themselves to be quite inactive. On the other hand, the evidence of Kauder is valuable, namely that single preparations found to be inactive can be made active in combination with other

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active substances. On this basis, disregarding the polyglandular limitations of senium præcox, the relevant treatment was that with a combination of all the glands of internal secretion. The patient received five tablets daily consisting of extracts of testicles or ovary, of placenta, of prostate, of liver, of adrenals, of thyroid and of pituitary and three times weekly an intramuscular injection to supplement the *per os* therapy. The successful result occurred after 3 to 4 weeks. The basal metabolism was raised, the specific dynamic albumin reaction was improved and the spastic atonic symptom complex of Müller was no longer demonstrable. The alveolar pyorrhea is on the decline, potency is increased.

Concerning the Changes in the Organs after the So-Called Regeneration Method. — Kornitzer. (*Med. Klin.*, **25** : 1387, 1929.)

The author maintains, according to his own experimental investigations, that the oral administration of desiccated substance of the testicle is better than the injection of testicular extract.

The opinion that the interstitial cells are the agents of incretory testicular function has been dropped by most authors.

Spleen Therapy in Bone and Joint Diseases. — H. Kuss. (*Med. Welt*, **3** : 1334, 1929.)

A report on the results of spleen therapy in seventeen patients. Daily dose about 100 gm. for 4 weeks, after a pause of about 3 weeks the spleen therapy was resumed. The author has it in mind to make concurrent investigations with spleen extract, but owing to a lack of suitable preparations this is not possible.

In ten of the seventeen patients an effect on the disease process was observed after spleen therapy, but it was not so great as the effect observed with general treatment. In six patients the condition remained practically uninfluenced, in three of these cases, in spite of the spleen treatment, a change for the worse occurred. Blood corpuscle pictures and the depression remained unaltered. In the great majority of cases an increased secretion of pus was observed. After a course of spleen treatment twice during 4 weeks, a definite improvement was seen in only three instances.

The Practical Significance of Hormone Therapy in the Treatment of Women. — Jaschke. (*Fortschrit. Therap.*, **5** : 565, 1929.)

According to clinical experiments the activity of the new sexual hormone preparations doubtless stands fast, and particularly with peroral administration. Failures rest either upon false indication or on insufficient dosage. First, as test for the effect attained is the menstruation-releasing or increasing activity as well as the growth effect; secondly, the regulation of the tempo of the cycle of intervention in cases of oligo- and hypomenorrhea.

Concerning the hormone of the anterior lobe of the pituitary, up to the present, useful mediums for practical application can not as yet be offered. The best results are to be had in secondary amenorrhea or in too seldom or too scanty menstruation of varied origin. A second important field of application is in cases of sterility in hypoplastic uterus. The preliminary results are only slightly satisfactory in primary amenorrhea, following high degrees of hypoplasia of the uterus. Yet, perhaps, in the future, still further success will be obtained with collaboration of the hormone of the anterior lobe. On the other hand, the sexual hormone exhibits pronounced service in climacterium præcox, the symptom of young, operatively castrated women. Striking success was obtained in arthropathia climacterium, however, the author warns against the administrations of preparations without due control.

Experimental Studies on Animals in Parabiosis, with Regard to Physiology and Biology of the Sex Hormone. — E. Fels. (*Arch. Gynäkol.*, **138** : 16, 1929.)

In a parabiosis between male and female the testicle degenerates first; contrarily, the ovary remains unaltered microscopically. In intense degeneration of the testicle castration symptoms are also evident in the pituitary. The assumption of an antagonism of male and female sex hormone is thus justified. On this score the female sex hormone may be considered the stronger biologically. The castrated parabiotic partner was not affected by the sex hormone of the normal animal. The cause of the genital changes in the normal animal in parabiosis with a castrated animal is the hormone of the anterior lobe of the pituitary of the castrated animal. The hormone of the anterior lobe of the pituitary

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passes over to the parabiosis partner more easily than the sex hormone. This observation is hence of practical significance, for in this case smaller doses are required to obtain the absolute effect or possibly, the hormone of the anterior lobe of the pituitary was not secreted so rapidly. Cramps in the non-pregnant parabiotic partner could be observed during the birth process in the companion, so the assumption of a toxin formed in birth must be declined.

In parabiosis between male and female conception and pregnancy only occur after total degeneration of the testicle. An already existing pregnancy was intercepted by means of the antagonism of the sex hormones, as long as a functionally capable testicle is present.

Contribution to the Ferment Theory of Acne and Furunculosis. — Ernst Less. (*Arztl. Rundschau*, **39** : 167, June 10, 1929.)

Furunculosis and acne often occur with disturbances of the digestive processes. Among the organs which supply the most important digestive juices is the pancreas. The internal secretions of the pancreas gland have an important effect on carbohydrate metabolism. For supplementing the pancreas ferment in furunculosis, therapy with living yeasts is particularly indicated. In the preparation of Vial and Uhlmann there is a combination of pancreas substance and yeast ferments with which the author obtained good results in the treatment of furunculosis and acne. The preparation shows itself to be a very good adjuvant through its power to greatly elevate the metabolism when used with local treatment with salves and radiotherapy for the treatment of furunculosis and acne.

The Process of Sterilization of Females. — A. Laffont. (*Gynécol. et obstet.*, **20** : 304, 1929.)

Noteworthy advances have been made in late years in the sterilization of animals by means of laboratory methods. It is possible to sterilize a laboratory animal temporarily with a subcutaneous injection of sperm. The sperm injection does not appear to act either on ovulation or on the ovary. It is possible that in this case a sterility is derived by means of sperm toxication of the uterine and vaginal secretions An attempt has been made to sterilize women by sperm injections; positive results appear to have been obtained here, but the process still stands in its infancy and is therefore not ripe for decision. The sterilization tests by means of ovarian extracts or transplants, as well as with placenta and fetal extracts lead to both short and long sterilization. By means of injection of corpus luteum disappearance of the menses and sterilization can be effected. Very interesting results have been reported with reference to this problem in women.

Folliculin acts to inhibit the nidation of the ovum, as has been seen in animal experiments.

Cotte in France and Vogt in Germany have shown with reference to insulin that in duration as well as intensity of menstrual bleeding, normally menstruating women undergo a decrease through the use of insulin. For this reason these authors have administered insulin treatment in menorrhagias of ovarian origin. Apparently the insulin takes effect on the ovarian follicle, thus inhibiting its development.

If the extract of the anterior lobe of the pituitary be injected into laboratory animals a sterilizing effect is derived; administered in weak doses the substance of the anterior lobe of the pituitary induces a rise in ovulation with increased activity of the whole genital tract. Given in large continuous doses the anterior lobe of the pituitary causes a follicular atresia with cystic degeneration.

Diabetes and Acromegaly. — Eric Martin. (*Rev. méd. Suisse Romande*, **49** : 693, 1929.)

Through investigation and study of pituitary extracts it has been possible to differentiate various substances of more or less definite activity; none of these substances, however, can be considered as the product of physiological secretion. On this score, the fact that the most active extract of this portion which is derived from the posterior lobe must be considered as particularly paradoxical. The anterior lobe which has a glandular constitution, supplies only slightly active products which, it seems, regulate the involution of the genital organs. Collin assumes that the so-called posterior lobe extract is the secretion product of the cells of the anterior lobe which accumulates in the intermediate zone and arrives in the region of the infundibulum. Recently it was actually possible for Abel to extract a crystallized substance from the

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posterior lobe as well as from the tuber, which possesses the characteristics of the pituitary extract.

Disturbances of sugar metabolism are usually found in diseases of the pituitary. In diabetes with acromegaly an ample explanation is found either through the hyperglycemic effect of the pituitary hormone or through tumor compression on the nervous centers of the infundibulum. On the other hand it is plausible to assume that these disorders are related through a hyperfunction of the pituitary with coincident alterations in the pancreas. There are cases of diabetes that may be considered as pluriglandular syndromes.

The Vegetative-Hormonal Regulation of the Skin. — Erwin Pulay. (*Wien. klin. Wochenschr.*, **42** : 1212, 1929.)

The significance of liver and spleen therapy for the treatment of skin diseases was extensively discussed and it was shown to what extent the determination of energy metabolism in association with the calculation of blood electrolytes affects the point of attack for treatment of skin diseases. The significance of the hormonal-vegetative system in conjunction with the splanchico-peripheral system was treated exhaustively. Information was given as to the effect of insulin and the experimental researches of Ernst Friedrich Mueller were minutely discussed.

The Sexual Hormone, the Placenta and the Newly Born. — E. Philipp. (*Zentr. Gynäkol.*, **53** : 2385, 1929.)

In the urine of the newly born there is found regularly from the first to the third day, a substance which can effect estrus in the castrated mouse, occasionally, in smaller amounts, up to the sixth day. This substance is found in the fetal ectoderm of human beings. Likewise, one can find in the urine of the newly born a substance which can induce the same changes in the ovary of an infantile mouse as does implantation of anterior lobe of the pituitary. This substance is identical with the hormone of the anterior lobe of the pituitary of the mother. The accuracy of the pregnancy reaction of Zondek and Aschheim, which is based on the excretion of this substance in the urine of the pregnant women, is confirmed. In the urine of a child a substance can be demonstrated which acts on the ovary of infantile mice by effecting ripening of the follicles and permits the consideration of an activity of the anterior lobe of the pituitary in the growing organism. The researches of the author extensively confirm the existing views on the basis of clinical observations, concerning the function of the placenta.

The Changes in the Endocrine Glands in Lead Poisoning. — Peisaschowitz. (*Virchows Arch. path. Anat. u. Physiol.*, **273** : 276, 1929.)

The lead accumulating in the blood induces atrophy of the thyroid gland, a weakened activity of the chromaffin system, an accretion of fatty substance in the adrenals and a diminution of formation of semen. The morphological changes which proceed in the incretory organs under the influence of lead poisoning, confirm the existence of a disturbance of the incretory equilibrium in the endocrine gland system.

Researches with Peroral Insulin in Diabetes Mellitus in Children. — M. Ottow. (*Münch. med. Wochenschr.*, **76** : 1584, 1929.)

In two young diabetics (14 and 15 years old) with 18 or 50 to 90 gm. of sugar in the urine daily, insulin preparations were given *per os* by Dr. Stephan and their effect observed. The result was slower than that with subcutaneous application. The disappearance of sugar from the urine precedes the decrease in blood sugar at one time. The preparation causes no harmful secondary effects. With gastrointestinal administration there seems to be an accumulation which effects an increased tolerance by means of further generation in the island apparatus.

Clinical Investigations on the Effect of Intravenous Insulin Injections. I. Blood Sugar Curves in Normal Individuals. — A. Norgaard and Th. E. Hess Thaysen. (*Hospitalstidende*, **72** : 881, 1929.)

The author applied the process of calculating the glucose metabolism under insulin effect which has the advantage of giving a direct index for the glucose amounts which the organism can metabolize under the influence of insulin as this potentializes the "degree of assimilation" or the "degree of tolerance." With the aid of this method one

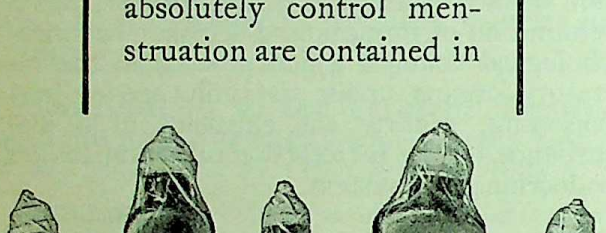
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DYSMENORRHEA

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can determine how much blood glucose in per cent, calculated per minute, can be oxidized after an intravenous injection of 12 insulin units. In nine men and nine women a typical curve was found after 12 insulin units. The first portion of the curve exhibited a decrease of blood sugar values, after the depression there followed a rise in values. These two portions of the curve the author indicated respectively as 1. "Transformation curve" which indicates the amount of glucose in the blood which is transformed under the insulin effect in the organism, and 2, the "Construction curve." The metabolism figures show in per cent the amount of glucose which was transformed in a minute from the blood glucose present before the injection.

The Adrenalin Content of the Blood in Narcosis. — H. Schlossmann and H. Mügge. (*Arch. exp. Path. u. Pharmakol.*, **144** : 133, 1929.)

The authors investigated the question of whether, during narcosis, the content of adrenalin in the blood stream is increased, and that by means of this the adrenalin impoverization of the adrenals is explained. The following was observed:

In the peripheral blood adrenalin is always first demonstrable when the blood pressure begins to fall. None of the narcotics investigated induced an exhaustion of adrenalin. The adrenalin exhaustion is rather an indirect effect of the narcosis and the result of decreased blood pressure. Following the termination of the narcosis the adrenalin exhaustion continues for a long time, even though the blood pressure promptly rises again. Under normal conditions adrenalin is not required to maintain blood vessel tonus, but immediately becomes vital when the normal regulation fails. Information has previously been presented by Delbet and Ogawa concerning the clinical significance of the impoverization of the adrenals directly by means of chloroform narcosis. Evidently by means of chloroform the new formation of adrenalin in the adrenals is inhibited.

Clinic and Therapy of the So-Called Hemorrhages of Puberty. — Runge. (*Med. Welt*, **3** : 1394, 1929.)

The author made therapeutic investigations with ovarian preparations but observed no success in his cases. This lack of success is due to the fact that the presence of this

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hormone in metropathia hemorrhagica is considerably higher in degree than normally. A hormone influence on this disease can only be accomplished if it is practically possible to derive the second ovarian hormone namely the secretion of the pregravid, transformation-effecting hormone of the corpus luteum.

Concerning the Hypophysin Therapy of Kidney and Ureter Calculi. (With Several Observations on the Motility of the Human Ureter.) — W. Schöndube. (*Zeitschr. Urol.*, **23** : 865, 1929.)

The reports of the few authors who have been occupied with the investigation of hypophysin therapy of calculi in the ureter as presented by H. Kalk, are not very encouraging. According to the author's investigations, despite the insignificant results of other authors, hypophysin seems to maintain its place in internal therapy as a supplementary medium. In 21 individual cases treated with hypophysin the author observed elimination of one or more concretions ten times, in one case three times within the course of a year. Hence in about 50 per cent of 21 cases a successful elimination of the calculus was obtained after hypophysin treatment, concerning which it may be said with reservations, that the therapy is usually to be combined with glycerin lemonade, several hours after the hypophysin injection, often also with ureter catheterization and water douches. In all criticism concerning post hoc propter hoc, it must be assumed, however, that in a portion of the cases mentioned the effectiveness of hypophysin injection in elimination of the calculus can not be gainsaid. In many cases, certainly, one derives the impression that hypophysin was quite ineffective, in spite of the fact that it had not been given in vain. The author thinks that the hypophysin by means of which he was able to observe increased ureter peristalsis cystoscopically, gradually disengages the calculus so that a douche is capable of dislodging the concretion. The result is that in many cases a very refractory calculus causes severe colic or pains after hypophysin, while a stone lying in the distal portion of the ureter, even with rather intense hypophysin peristalsis, seldom causes colic. In severe septic disease symptoms the author bars the use of hypophysin treatment. Hypophysin is no medium for promoting spasms, but rather a substance which enhances the normal course of the peristaltic process, in contrast to pilocarpin (Katsch). In kidney calculi the indication for hypophysin therapy is less favorable than in cases of ureter calculi.

Several Investigations into the Effects of Thyroid Gland Preparations. — Shimazono. (*Klin. Wochenschr.*, 8 : 1789, 1929.)

The injection of thyroxin into the lymph system in rabbits, in one-tenth the dose, acts on basal metabolism one hundred times as strong as the intravenous dose. The action is not altered by severing the cervical sympathetic. On the other hand, injection of thyroxin into the lymph has no effect on the water metabolism. A direct influence on the metabolic center was assumed, which is certainly evident since the tissue respiration of isolated tissue is not changed by thyroxin. Also hypophysin acts in the lymph much more strongly than in intravenous application. In suitable dosage thyroid gland preparations promote the regeneration of peripheral nerves, which was proved experimentally on the ischium and therapeutically in polyneuritis.

Contribution on the Calculation of Quantities of Sexual Hormone. — Siebke. (*Zentr. Gynäkol.*, **53** : 2450, 1929.)

The presentation of a scientific, objection-free and successful hormone therapy is the knowledge of the hormone quantities with which the body normally functions. In addition, it is important to know directly in which diseases there is a lack and which an excess of hormone. During the menstrual cycle the hormone concentration in the blood reaches its height on the 3rd day before menstruation. Hence, therapeutic doses of hormone as supplement give the best results from the 12th to the 3rd day before the expected menses, or the 17th to the 26th day of the 28 day cycle.

In the circulating blood of the normal woman during the menstrual cycle there is found from less than 100 mouse units to more than 200 mouse units of hormone. During pregnancy the hormone concentration in the blood rises higher than during the cycle. The determination of hormone in the blood of amenorrhea subjects confirms the fact that there are fluctuating cycles. According to the results of the author indication is given of the height of the fluctuating curves of hormone therapy. In cases of metropathia

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hæmorrhagica the sex hormone content of the blood may be increased in the period between and hence the therapy with sexual hormone is unsuitable. During the first week of the metropathic hemorrhage the hormone concentration in the blood is raised, hence a therapy with sexual hormone is not applicable.

Internal Secretion and Psychic Processes. I. Hormone Reflexology. — W. N. Speranski. (*Abhandl. a. d. Neurol. Psychiat. u. ihren Grenzgeb., Monograph*, No. 52 : 1, 1929.)

The "emotiogenic" (em.) hormone is in the main the derivative of the hormone. There is every reason to assume that, for example, the "disquiet-emotion" is linked with the activity of the thyroid gland. After continued mental excitement associated with a feeling of anxiety an important increase in the size of the thyroid gland may be observed. Imbecilic quiet has been observed in myxedema.

The hormone of the sex glands has a general stimulating effect on the organism and possesses no emotional properties. However, under certain other influences an excessive reflex decomposition of this hormone may occur which induces an erotic emotion.

Cannon reported on an increased amount of adrenalin in the blood of infuriated cats. Adrenalin itself possesses no "emotiogenic" property. The manifestations of cyclothymia, the maniacal depressive psychosis are associated with cyclic disturbances of the equilibrium in the system of hormone formation. If hysteria is dependent upon an underdevelopment of a portion of the nervous-psychic apparatus, associated with the underdevelopment of several hormone-forming organs and coordinations in the system of hormone formation, then the catatonia of puberty may be explained as a premature development of a portion of the nervous-psychic apparatus (including the hormone producers).

Concerning the Peroral Action of Insulin and Peroral Insulin Therapy. — Richard Stephan. (*Münch. med. Wochenschr.*, **76** : 1579, 1929.)

The author conducted very extensive researches on the peroral administration of insulin. For administration in mechanically suitable dispersion preparation dry insulin or insulin salt, suspended in a digestible fat or oil colloidal and in various admixtures, was given on an empty stomach. It was thus demonstrated that with peroral administration, the essential condition for resorbability is fulfilled in prompt release of the bile reflex and in intrastomachal presence of an insulin-bile acid relationship. The bile-acidic insulin requires no protection, it is not destroyed in the fasting stomach. In experiments with diabetics it was shown that the true insulin effect occurs after the ingestion of food. Peroral insulin administration discloses a rather important deposition effect in the organism which, as opposed to all experiments thus far, is to be considered novel, in other words, that in the fasting period total insulin effect is in no wise obtainable.

For the individual case there exists an optimal peroral dose which has the maximum effect on the blood sugar curve.

The results of the author permit the affirmation of the value of peroral insulin therapy.

Internal Secretion and Internal Medicine. — W. H. Veil. (*Fortschrit. Therap.*, **5** : 564, 1929.)

The hormone has been developed into a very favorable adjuvant remedy. In handling it the practicing physician must consider that the hormones are related to definite organs which give rise to them, that they do not merely serve as substitute preparations for these organs or the lack of their function. Only in a small number of cases must substitution be made with hormones. The classical examples in this instance are the substitution of thyroid gland function and of liver function in pernicious anemia. On the contrary, insulin is not precisely a therapy for diabetes.

The hormone can be employed for therapeutic effect quite dissociatedly from the fundamental activity of the internal secretory gland, thus the hormone of the thyroid gland can be used in treatment of emaciation, etc. The interrelation of hormone therapy and plant poison therapy is important. Adrenalin, for example, by relieving the unfavorable influence of digitalis on the respiratory organs, can produce a favorable result in digitalis therapy. Likewise, adrenalin can relieve kidney contraction due to the action of digitalis. In the heart itself adrenalin can aggravate the transfusion from auricle to ventricle and even inhibit it (heart block). Thyroxin is capable of dispersing this unfavorable effect.

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Hormone therapy must also be administered with very careful observance of the unit content. The author reports that in one case of pernicious anemia the condition was brought to one of sugar disease by means of the administration of raw liver. This unsatisfactory result was explained thusly: that in raw liver there is present another hormone besides the one with favorable influence on pernicious anemia, namely the glycemin discovered by Loewe. The occurrence of the sugar disease in this case is to be ascribed to the action of the glycemin.

Is It Possible to Influence the Internal Secretion of the Pancreas Operatively? — R. Demel and E. Krammer. (*Mitt. Grenzgeb. Med. u. Chir.*, **41** : 582, 1929.)

On the basis of animal experiments the authors come to the conclusion that the internal secretion of the pancreas is not to be influenced operatively, at least as far as is known by present methods. There is hence no claim, provisionally, to apply this process to human beings.

Hemorrhages during the Change Years. — B. Wolff. (*Zeitschr. ärztl. Fortb.*, **26** : 591, 1929.)

Occasionally good results were obtained with pituitary preparations of various kinds. In addition, ovarian preparations and a local therapy with dabbing of the cervix with adrenalin was instituted.

Experimental Investigations on the Physiology of the Genital Tract in Females. — Rudolf Dyroff. (*Arch. Gynäkol.*, **138** : 362, 1929.)

From the corpus luteum or the ovary all sorts of chemical derivatives have been obtained which actually cause the formation of more or less artificial decomposition products, which must not be placed on the same basis as the true internal secretion because they are capable of exercising a more or less specific biological function. This likewise holds true for the new ovarian preparations of Zondek and E. Laquer, though with these, in amenorrhea cases, normal menstrual processes were initiated more often than previously with similar extracts and although the author himself was able to induce a uniformly increased genital plasia with these in rabbits. At any rate the Zondek preparation evidently contains the hormone of the corpus luteum in higher concentration than formerly, however, one must not exhibit this as an estrous hormone, for estrus, and also ovulation, was not induced, but rather a hyperemic process in the genitals.

Knowledge concerning the histological-chemical similarity between corpus luteum and adrenal cortex has long been obvious. (Mulon and Wallart.) Mulon goes so far as to say that the corpus luteum is a temporary adrenal cortex. However, indications accumulate that one has to look for the physiological counterpart of adrenalin for the tonus of the parasympathetic in the body in the secretion of the adrenal cortex. Cholin is to be regarded as the physiologic parasympathicotonic for the intestine. As proof of the possibility of a similar internal secretory effect of corpus luteum and adrenal cortex, the fact may be presented, too, that pubertas præcox occurs with tumor of the cortex of the adrenals. As an outcome of this the whole strikingly fine development of the female genitals in the newly born (excessively large adrenals) is comprehensible. Whether the disputed internal secretion of the corpus luteum belongs to the cholin group is undecided. However, we have here a secretion which has specific parasympathicotonic properties.

Hypophyseal Diseases. — F. Boenheim. (*Zeitschr. ärztl. Fortb.*, **26** : 617, 1929.)

The hormone of the pituitary exercises an extensive influence on the collective organs of the human body. Very often disturbances of growth attend diseases of the pituitary. In pituitary dwarfism the therapy is generally little effective. Falta recommends the injection of extract of the anterior lobe in the so-called third growth period, *i. e.* after the 13th year of life. For genital dystrophy this medication is almost always invalid for human beings. In dystrophia adiposogenitalis pituitary preparations have been given repeatedly, particularly in combination with thyroid gland. Though Falta states that only severe dietetic cases are to be influenced, this does not coincide with the author's opinion. The importance of the pituitary for the circulation is definitely determined. The pituitary hormone presents a factor for the regulation of blood pressure. By injections of preparations of posterior pituitary it is possible to increase the blood pressure. Further, the possibility

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of inducing contractions of the gall bladder by means of pituitary preparations is therapeutically important. The same holds true for the intestines, so that striking results may be obtained in many spastic forms of obstipation. The influence of pituitary preparations on diuresis in healthy and diseased individuals is not effective with peroral dosage, but is efficacious in injection and in rectal administration in the form of suppositories, of which fact the author was convinced by a whole series of tests.

The Gottlieb School relates paradentitis to disturbances of the pituitary (Weinwann) which, however, occurred in only one-fourth to one-fifth the author's cases.

Relation between Age and Thyroxin Activity. — E. Abderhalden and E. Wertheimer. (*Zeitschr. ges. exp. Med.*, **68** : 1, 1929.)

From the investigations of the authors it is shown that the activity of thyroxin, measured with regard to body weight and age, is in close relation with the age of the animal. With increasing age the thyroxin effect, in the relation mentioned advances more and more. The loss of glycogen is accomplished more slowly in growing animals than in adults. Young and adult animals, in general, lose fat in the same degree; likewise with regard to gas metabolism and nitrogen metabolism no difference was observed in both young and old animals with respect to thyroxin effect.

Concerning the Female Sex Hormone, Menformon, Particularly Its Antimasculine Effect. — E. Borchardt, E. Dingemanse, S. E. de Jongh and E. Laqueur. (*Zeitschr. ges. exp. Med.*, **68** : 86, 1929.)

By means of menformon the primary and secondary sex characteristics, in development as well as formation, are influenced in a negative sense. The inhibition is transient and after termination of the treatment is capable of totally disappearing. The antimasculine influence is particularly demonstrated in rats, guinea pigs and rabbits. In young animals about 1 mouse unit per day suffices to institute inhibition after 5 weeks. The "all or nothing" law does not hold with regard to menformon activity, on the contrary the question of dosage is of greatest importance for the strength of the effect. Steinach's evidence that the occurrence of an inhibition of the secondary male sex characteristics in the presence of the testicle with normal formation of semen only signifies that the antimasculine effect immediately seizes upon the genitals themselves, does not seem to the author to be established. The influence of menformon on the male sex organs is specific, for it is not to be observed in any other organs. Mammary and adrenals are augmented. The investigations of the author testify that the inhibiting effect passes over to the testicle.

Concerning the Significance of the Spleen and of the Radial Cell System (Reticulo-Endothelium) for the Prophylaxis of Malignant Inoculation Tumor in the Rat. — B. E. Brüda and H. Pfeiffer. (*Zeitschr. ges. exp. Med.*, **68** : 116, 1929.)

The spleen as well as the rest of the radial cell system (reticulo-endothelium) contributes to the true endocrine glands. In the investigations on rats, part singly and part in parabiosis arrangement, it was shown that the spleen effects a prophylaxis and inhibition of the progress of malignant mouse tumor in the rat. Since this prophylaxis, as has further been shown, is to be considered as the display of a chemically active inhibiting substance, as an internal secretory process, thus the reticulum of the spleen belongs to the endocrine glands.

Concerning Resistance to Thyroxin. — W. Falta. (*Endokrinologie*, **5** : 62, 1929.)

In treatment with thyroid gland tablets it is possible to observe that the effect on individual test persons is often quite varied. The author made observations on a case with symptoms of the central nervous system, which gave definite evidence for the diagnosis of polioencephalomyelitis; this case appeared fairly refractory to large doses of thyroxin or thyropurin. A rise in pulse frequency occurred, but the basal metabolism was not at all changed. The author also observed a second case of resistance to thyroxin, a case of status postencephaliticus. There are animal experiments concerning this, which demonstrate a relation between the resistance to thyroxin and the nervous system. Clinic and experiment demonstrate the possibility that in highly differentiated organisms the metabolism-increasing effect of thyroxin is suppressed according to the conditions of the central nervous system.

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On the Treatment of Psoriasis with Products of Digestion of the Cutaneous Scale. — Vojislav Mihajlovic. (*Wien. klin. Wochenschr.*, **42** : 1192, 1929.)

In the rather inadequate knowledge we have so far concerning the etiology of psoriasis, one must not be surprised that the therapy of this disease is not yet placed on a firm basis and that the physician is thus left to a manifold therapy, in which, not infrequently, he has the sad experience of observing that in very severe cases the disease resists all sorts of variously recommended and applied therapeutic remedies. Such a severe case of the disease gave the author the idea to study a treatment with extracts derived from the skin scale, similar to that which Strümpke (1921) and Vercellino (1924) have done. The author then proceeded immediately in collaboration with Professor Joannovíc in the Institute for General Pathology and Pathological Anatomy, to the application of one of his methods of digestion of scale with pepsin and trypsin by means of the extracts produced by Dr. Tichomirow.

On the basis of 15 months of experimentation in the treatment of psoriasis with digestive products of psoriasis skin scale, according to the method derived by Joannovíc, the author states as follows:

"1. The subcutaneous injection of this preparation brings forth neither local nor general reaction.

"2. At the beginning of treatment an intense skin irritation occurs, while the efflorescence begins to scale slightly and abruptly.

"3. In the process of treatment no characteristic punctiform hemorrhage occurs with removal of the efflorescence and with cessation of the irritating skin symptoms.

"4. The flexing of the joints, painfully hindered by the skin changes, returns again to normal with cessation of the pain.

"5. The leukodermia occurring on the site of the efflorescence, is coincident in form with the efflorescence and is to be differentiated from a leukodermia following chrysarobin. Though leukodermia psoriaticum is extraordinarily seldom, it belongs as a rule to this sort of treatment.

"6. The efflorescence usually disappears first from the scalp, then from the skin of the breast and the abdomen. The changes in the knees and elbows are most resistant as is also the case with other methods of treatment.

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"7. The injections are given subcutaneously, daily or every second, third, fourth or fifth day, in amounts of 1.0 to 5.0 to 10 cc. and are tolerated entirely without reaction. The digestive product given need not originate with the patient himself, but may be successful even if derived from the skin scale of other patients; however, the autologous extracts seem to be the more effective.

"8. This method of treatment, above all others up to the present time restricts the occurrence of relapses."

The results obtained up to the present with this method of treatment, warrant considerable attention and further trial in order, if possible, to obtain still better and more lasting results with it.

The Treatment of Rheumatic Diseases. — A. Zimmer. (*Fortschrit. Therap.*, **5** : 545, 1929.)

Ovarian, thyroid and pituitary are preeminently the glands the disturbances of which can definitely be associated with the cause of rheumatic diseases. Obesity is closely allied therewith. Hormonal therapy in disturbances of internal secretion is not to be regarded as a substitution therapy, but as a causal treatment, for it has been shown that there is involved here not a substitution alone, but a definite length of treatment in order to obtain a restoration of the equilibrium of the internal secretion function.

The Significance of the Thyroid Gland for the Pathogenesis and Clinic of Basedow's Disease. — Georg Büttner. (*Brun's Beitr. klin. Chir.*, **147** : 623, 1929.)

Asher concludes from the varied activity of the thyroid gland secretion that the thyroid gland hormone is the activator of the vegetative automatism. Asher conceives the division of work between adrenalin and thyroxin in such a manner that the thyroid gland secretion is effective as activator in the same places where adrenalin is a stimulant toxin. The adrenalin effect is a rapid, progressive nerve stimulation, thyroxin effect begins slowly and ends slowly. It is not yet known how the combined action of adrenalin and thyroxin takes place. The strongest argument against the thyroid gland theory of morbus basedowi is the impossibility of creating a total Basedow condition experimentally. The acute feeding tests, even with large doses of thyroid are to be considered invalid, the chronic lengthy feeding experiments are not uniform.

If one administers thyroid gland substance in the presence of thyroid gland, to induce an experimental hyperthyroidism, substitution occurs as in myxedema, the incretion substance introduced is not a simple addition, but rather occasions an altered milieu in the organism, which is also supported by the thyroid gland passively.

Arterial Hypertension with the Symptom Complex of the Left Heart. Treatment by Means of a Pancreas Extract. Improvement. — H. Chabanier and P. Truchot. (*J. Urol.* (*French*), **28** : 405, 1929.)

In a 50 year old female patient with hypertension and intense insufficiency of the left heart an unequivocal improvement of the condition was obtained by means of a treatment which consisted exclusively of the administration of pancreas extract. The functional as well as anatomical symptoms which were dependent upon a dilatation of the left heart, showed a very prompt and significant decrease, though the hypertension only first exhibited a retrogression about 6 weeks after commencement of the treatment. It must also be pointed out that the treatment may be sustained without the appearance of any secondary symptoms whatever. On the other hand, report was made previously of the therapeutic effect of various pancreas extracts, some insulin and some other extracts, in hypertension with symptoms of insufficiency of the left heart.

Ovarian Insufficiency with Oligo- and Hypomenorrhea. Pregnancy after Treatment with Extract of the Anterior Lobe of the Pituitary. Disappearance of the Symptoms of Ovarian Insufficiency. — G. Cotte. (*Bull. Soc. obstét. et gynécol.*, No. 8 : 559, 1929.)

A 20 year old female patient came to the author in September, 1927, for treatment. The patient was menstruating scantily, was very fat and showed unquestionable symptoms of endocrine disturbance. Menstruation was irregular, seldom and very painful. The attempt with transplantation of ovarian substance failed, because the transplant was ejected. Finally a test was made with injection of extract of the anterior lobe of the pituitary. In the month following the patient spontaneously reported that she felt much

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better and that she had become pregnant. Since the commencement of pregnancy (4 months) the findings are very good. Without desiring to draw too extensive conclusions from these results, the author thinks that the administration of substance from the anterior lobe of the pituitary deserves consideration. Since the appearance of the publication of Zondek and Aschheim it is known that the anterior lobe exerts a specific and also a stimulating influence on the genital apparatus. It is possible, in animals, by means of injection throughout one day to obtain hypertrophy of the genital tract. The observation of the relation of the follicle of the corpus luteum after injection of the anterior lobe of the pituitary also gives the author the opportunity to treat cases of amenorrhea with injectible extracts of the anterior lobe of the pituitary. At any rate, in cases in which ovulation is lengthy, sluggish or insufficient, the method of administration of anterior lobe extract is to be preferred to that of other substances of endocrine gland origin.

The Nervous Disorders of Biermer's Anemia, and Liver Therapy. — H. Curschmann. (*Münch. med. Wochenschr.*, **76** : 1863, 1929.)

Since the initiation of liver therapy no improvement was seen in the spinal syndrome in pernicious anemia. The effect of liver therapy on the nervous disorders is totally negative. There was neither improvement of the objective symptoms nor of the subjective disturbances, more often there was an increase in the spinal symptoms. Liver therapy failed totally as far as concerned the nervous disturbances.

Hyperthyroidized Animals and Their Progeny. — G. Döderlein. (*Zentr. Gynäkol.*, **53** : 2594, 1929.)

Different authors in recent times propose the administration of incretory organ preparations (insulin, thyroidin) in diseases of metabolism in pregnancy (Dyroff, Gessner, Kermauner, Klaften, Kraul have published such work). Up to the present only very carefully allotted doses have been given, for a short time only, and only at the termination of pregnancy, in order that the symptoms of the actual disease in the mother could be sufficiently influenced without harming the fetus any more. The endocrine therapy may be administered in large doses harmlessly, if a transfer of the substituting hormone to the fetus, and thereby the possibility of harming the fetus, is not to be feared.

This question may be tested in warm-blooded animals. The warm-blooded animals are not to be compared, in their bodily functions, with human beings, but conclusions from animal experiments are permissible. Döderlein has found that in experimental hyperthyroidism the hyperthyroid condition, brought about by a large dose of thyroidin, suppresses propagation in very fertile animals. In the second generation there is remarkable sterility in male offspring of hyperthyroidized animals.

Endocrine therapy is a totally different method of treatment. On this account one must be cautious with application of this therapy in pregnancy, where the fetus also may be affected.

Concerning the Effect of Thyroxin on the Iodin Content of the Blood in Myxedema Patients. — B. Eisler and A. Schittenhelm. (*Zeitschr. ges. exp. Med.*, **68** : 487, 1929.)

The iodin content of the blood in myxedema is very much decreased. Thyroxin is effective in increasing the iodin content of the blood and the basal metabolism. The iodin content of the blood rises to values above normal as soon as the thyroxin effect sets in and in spite of continued thyroxin dosage falls to roughly normal values. There is no parallel between basal metabolism and iodin content of the blood in myxedema patients during the administration of thyroxin. The iodin concentration of the blood of normal persons is not increased after prolonged application of thyroxin.

Report on the Principles of the Male Hormones. — O. O. Fellner. (*Endokrinologie*, **5** : 66, 1929.)

There are at least two male hormones; one male hormone, the counterpart of the female, is the substance which brings about the eventual formation of the male sex characters; its seat is evidently the testicle. The second hormone brings the testicle to maturity and maintains the mature state. Similar to Smith and other contributors the author observed hypertrophy of the interstitial cells, augmentation of the seminal vesicles and growth of the penis following

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injection of the hormone of the anterior lobe. Even with very large doses, injected over a long period of time, the author could not derive maturation of the testicle. According to the experiments of Biedl and Aschner it must be assumed that in the pituitary, in the anterior, intermediary or posterior portion, a hormone was produced which is the impulsive force for the male sex hormone. But this is certainly not identical with the anterior lobe hormone. From his own experiments the author concludes that the gonads are hermaphroditic in regard to secretion, that unquestionably there must be two hormones. The author presents observations on a male whose breasts were fully developed as those of a woman.

The author was able to demonstrate without difficulty that the interstitial cells of the normal ovary produce the female sex hormone. Whether the female hormone derived by the author from the testicle is from the interstitial cells is not yet accorded, however, Fellner holds it as evident. Pseudohermaphroditism and sex modifications therefore, seem to be based upon the fact that between the gonads and the superseding organ there exists a dysfunction.

Corpus Luteum and Sexual Hormone. — L. Fraenkel and E. Fels. (*Zeitschr. ges. exp. Med.*, **68** : 172, 1929.)

The hormone which releases estrus in the castrated mouse is evidently not the female sex hormone. Doubtless it is an important constituent of the female sex hormone. It is the follicular hormone and is also found in the corpus luteum. Moreover, in corpus luteum there is another hormone component which can not be demonstrated by means of test objects and which is not yet presented in manufactured form.

One gains an insight into the question of identity of sexual hormone and corpus luteum incretion from experiments in the clinic. One must firmly grasp the fact that a valuable hormone which contains all the physiological potentialities must also lead to successful therapy as in the case of insulin, thyroidin and adrenalin. It is another matter with the sex hormone preparations. There is no doubt that they are effective in test animals; on the other hand the clinical results, viewed favorably, are to be considered at most mediocre. They are practically null in the case of sterility. The end result and termination of each hormone therapy is the pregravid construction of the mucous membrane of the uterus and the forced menstruation following therefrom. L. Fraenkel in 1927 mentioned 30 per cent results on this score, at best, and he expected an increase in the number of successful outcomes, but the expectation was not fulfilled. The results are very bad in the case of primary amenorrhea, as v. Jaschke has recently emphasized. However, very good results have been obtained with corpus luteum preparations in insufficiency symptoms and sometimes also even in cases of amenorrhea. It will be the task of the future to seize upon all the hormone components and to apply them therapeutically.

Parabiosis and Anterior Lobe of the Pituitary. — H. Kallas. (*Pflügers Arch. ges. Physiol.*, **223** : 232, 1929.)

From parabiosis experiments it is shown that the infantile pituitary produces hormone of the anterior lobe and is capable of giving it off into the blood, and further, that the ovary influences the endocrine activity of the anterior lobe of the pituitary.

Menstruation and the Hormones of Ovary and Anterior Pituitary

(*Continued from page 271*)

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Concerning the Hormone of Heart Motion. 13th Contribution. — L. Haberlandt. (*Zeitschr. ges. exp. Med.*, **68** : 185, 1929.)

The author investigated further concerning the heart hormone preparation and determined the super-limits of activity for adrenalin- and histamin-free heart hormone preparations in dilution of 1:100 millions to 1:1000 millions (in 0.5 cc. liquid). With these concentrations on a suitable sensitive heart, the pulse-inciting and pulse-accelerating effects of normal heart stimulation substance could be demonstrated. By means of lengthy application of the heart hormone preparation, according to conditions, the excitability of the frog ventricle is abbreviated.

Concerning New Substances with Insulin-Like Effects. (Biguanidin and Its Derivative.) — E. Hesse. (*Münch. med. Wochenschr.*, **76** : 1697, 1929.)

In biological relationship biguanidins have many characteristics in common with synthalin-like substances—polymethylen-diguanidin, as the symptom of blood pressure decrease, hypoglycemic cramps, the initiation of these with grape sugar and the impossibility of alleviating the cramps with adrenalin. Regarding glycogen synthesis in normal animals as well as those deprived of the pancreas, this experiences no difference. On the contrary the effect of insulin on glycogen synthesis is basically different, for with insulin the relief of the insulin cramp with adrenalin, the life-saving effect of grape sugar and above all the characteristic trophic influence of insulin on the dog without pancreas, by which the animal is kept bright, lively and healthy, is evident. All these things are unattainable with biguanidins. This fact is of great importance in therapeutic application of these substances to human beings.

The Functional Relation between Pituitary and Pancreas. — B. A. Houssay. (*Endokrinologie*, **5** : 103, 1929.)

There are two groups of definite and important facts, namely, on the one hand the mutual antagonism between extract of the anterior and posterior pituitary lobes and insulin and on the other hand, the great sensitivity of hypophysoprivic animals to the hypoglycemic and toxic effect of insulin which may be inhibited by means of injection of pituitary extract. Burn noticed that with pituitary extract the glycemia inhibited by the effect of insulin receives a new impetus and the hypoglycemic symptoms can be made to disappear. The extract of the anterior lobe of the pituitary does not have the antagonistic effect of pituitrin. The effect of the posterior lobe extract is specific. Bollinger and Hartmann confirm the experiences of Winter and Smith, that insulin offsets the organic blood phosphorus and the extract of the posterior lobe increases it. Progressive doses of insulin restrict the oliguric action and the hydremia induced by a later injection of posterior lobe extract in laboratory animals and in human beings with water diuresis. According to Pogany and Pinter-Kövats, the injection of insulin before that of posterior pituitary incretion lessens or restricts the arterial blood pressure-increasing effect of the posterior lobe extract. According to La Barre the injection of pituitary extract augments the secretion of insulin.

The Influence of the Anterior Lobe of the Pituitary on the Genital Tract in the Guinea Pig. — J. Watrin. (*Bull. Soc. obstét. et gynécol.*, No. 8 : 574, 1929.)

On the basis of implantation tests on guinea pigs the author was able to derive the following results:

The genital reaction on the part of the pituitary hormone is of a quantitative and not of a qualitative nature. Large amounts of hormone effect very great changes. The uterine reaction is identical with the ovarian or is exactly dependent upon it. The observations of the author are a confirmation of the experiences of Courrier and Kehl, who by another method, namely by injection of increasing doses of pituitary extract obtained alterations which are proportional to the size of the dose.

Gregor Johann Mendel

(*Continued from page 279*)

altercations with political personalities. A final conflict with the German Liberalist Party, especially concerning the property of the religious institution, which he fired with numerous protests, culminated the difficulties of this defiant, liberal-minded abbot, and there began to be surreptitious remarks concerning

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the sanity of his mind. Life became increasingly uncomfortable, with only his nephews and close relatives to cheer him, for they knew and appreciated his idiosyncrasies. On January 6, 1884, rather suddenly, Mendel died of organic heart trouble with complications.

Mendel's place in the scientific world is very definite. Besides being a careful research worker he was a profound thinker. His manner of living particularly suited the work he chose, for the well regulated, easy-flowing life of the monastery offered an excellent setting for the long and tedious experiments which formed the basis for his system of heredity. His contributions to the literature are few: specifically, "Experiments on Plant Hybrids," first published in 1865, and "Meteorological Observations." Letters (published in 1905) to his friend Carl W. v. Nägeli the botanist (written during the years 1866 to 1873) give evidence of the trend of the work on heredity, to which Nägeli often lent inspiration and guidance.

One can not describe Mendel's work on heredity briefly. Fundamentally, however, the work was done on the common pea. His method, unlike other students of this problem, was to trace a single pair of alternative characteristics at one time. He crossed a tall and a dwarf plant and carefully followed the appearance of these two factors alone. The same method was applied to other plants, and likewise, though not so detailed, to animals. He chronicled the results of these experiments. From these excellent researches biologists have been able to extend the application of the principles to unnumbered problems, and thus there has come into the annals of science a "New conception of the nature of living things — and of their potentialities and their limitations." Great economic value has been derived from Mendel's work, also, for it is evident that the breeder of plants or animals is enabled to obtain definite and excellent results if he follows the fundamentals discovered by Mendel.

Unlike the work of Darwin who received immediate recognition from the scientists of the period, Mendel's almost disappeared, for exceedingly little was known of it until 1900, when it was rediscovered by deVries, Correns and Tschermak; but with the resurrection of his work such prompt and extensive advances were made as a result of the knowledge he gathered, that Mendel's fame is now no less than Darwin's.

Liver Diet and Reticulocyte Reaction in Simple Anemia. — J. Wahlberg. (*Acta med. Scand.*, **72** : 143, 1929.)

The author reports on the clinical investigations regarding blood regeneration in simple anemia under liver diet, as compared with the erythropoietic reaction of iron and arsenic therapy and hospital treatment without special therapy. The sick material observed consisted of 19 cases and 8 post-hemorrhagic anemias, 5 patients with achlorhydria (of whom one evidently had carcinoma of the stomach) 3 patients with hypochromic anemia with parasitic infection.

Of 15 patients 9 reacted well to liver diet in which processes there was no difference in therapeutic effect either with liver extract or liver feeding. In 3 cases better results were derived with liver diet than with iron and arsenic therapy. In a few cases the effect of iron and arsenic therapy was not augmented by liver dosage, in several cases iron and arsenic therapy succeeded better than liver therapy. The author comes to the conclusion that liver therapy in simple anemia should be tried in those cases which do not react to iron and arsenic, particularly in cases of post-hemorrhagic anemia and other conditions of long duration.

A Case of Post-Partum Hemorrhage. Medical Treatment. Cure. — Voron and Banssilon. (*Bull. Soc. obstét. et gynécol.*, No. 8 : 569, 1929.)

A case of a tertipara in good state of health, with sudden initiation of birth en route to the hospital, abundant lochia, from the 3rd day on intense hemorrhage with the elimination of large clots. The patient received injections of pituitary extract but only a very weak effect was obtained with these. Only with subcutaneous application of ergotamin was cessation first obtained. The patient left the hospital cured.

Fetus and Vitamin A. — E. Vogt. (*Münch. med. Wochenschr.*, **76** : 1748, 1929.)

Vitamins and endocrine glands are dependent upon each other. In rats keratomalacia occurs more promptly if one feeds thyroid gland substance simultaneously. The antisterility vitamin, E, and the ovarian hormone must be closely related for their activity is extensively dependent upon each other. Insulin and radiated ergosterin are

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very similar to each other physico-chemically. The author made tests on fetuses and found that Vitamin A can be determined in various stages of development in the liver in fetuses. However, Vitamin A was demonstrated in no other organ. From the exclusive presence and the storage of Vitamin A in fetal liver it is possible to estimate how important this organ is for vitamin metabolism in the fetal organism.

On the Question of the Possibility of Influencing the Effect of Thallium by Means of Extracts of Endocrine Glands, with Especial Reference to the Thymus. — Y. Vásárhelyi. (*Dermatol. Zeitschr.*, **56** : 412, 1929.)

The ingestion of active substances of the endocrine into the organism offers difficulties in that these substances are very sensitive to the salt acids of the stomach. In previous experiences the author observed that with the administration *per os* of fresh glands or of tablets no decisive effect could be expected and has therefore worked partly with extracts and partly with transplantation. The experiments were conducted on white rats; as indication of the effect of thallium the initial falling out of the hair was used. In animals which received besides 0.0002 gm. thallium daily, 0.5 cc. ext. testiculi or a similar dose of ext. ovarii, no influence of the sex gland extracts on the thallium poisoning was to be observed. In animals which received in addition to 0.0002 gm. thallium daily, 0.5 cc. of ext. thymus subcutaneously the falling out of the hair occurred much earlier than in the control animals treated with thallium alone and made definitely more rapid advances than in those thallium animals not treated with thymus extract. In the latter total baldness occurred on the 120th to 130th day, in the thymus animals on the 105th to 115th day. The author assumes that hyperthymization influences the effect of thallium positively. V. Berde came to the same conclusion. This condition explains also the observation that young organisms are considerably more sensitive to thallium.

Concerning Thrombosis and Embolism. — A. Mayer. (*Zentr. Gynäkol.*, **53** : 2770, 1929.)

It would be best to avoid thrombosis by means of prophylaxis. Unfortunately the mediums suitable are few and judgment of the effect is difficult. However, along with preliminary treatment by means of digitalization prophylactic thyroxin treatment also deserves consideration. According to Walters at the Mayo Clinic with 1745 patients under 70 years of age in large operations during two years no embolism was observed. The author gave no information on the amount of thyroxin treatment.

Is There a Form of Amenorrhea Which Can Be Caused by a Constitutionally Underfunctioning Thyroid Gland? — H. Toronczyk. (*Monatsschr. Geburtsh. u. Gynäkol.*, **83** : 167, 1929.)

A report on 12 cases of amenorrhea during the ages of 18 to 39 years, in which, regarding the genital findings it was to be assumed that barring the lack of menstrual bleeding, all other internal secretory functions of the ovary were in good condition. All 12 women were treated with thyroid and prompt success ensued. Most authors are in accord with the knowledge that the corpus luteum exerts a direct inhibiting effect, or as others believe, a neutralizing effect against thyroid. When the reformation of corpus luteum occurs and fails to exercise its inhibiting effect on the thyroid, as direct effect of this syndrome an initiating, always advancing intensification of thyroid gland activity must be assumed. If one takes the point of view that the stimulus to menstrual bleeding arises with the thyroid, the rôle of the corpus luteum at the commencement of pregnancy is clearer. Those cases of edema of pregnancy which are successfully treated with administration of thyroidin, can perhaps be caused by a too strongly developed mammary gland (hence a too strong inhibition of the thyroid gland). Cases of habitual abortion which were treated successfully with small amounts of iodin give evidence that in these cases there is a question of dysthyroidism. From experiments it is known that many dysfunctions of the thyroid gland can be influenced by small doses of iodin.

On the Effect of Several New Circulatory Mediums in Insufficiency of Blood Circulation. — P. Trendelenburg. (*Med. Klin.*, **25** : 1505, 1929.)

The insufficient heart can often be rendered promptly sufficient by means of ephedrin-ephetonin and the related adrenalin. The volume per minute increases, the auricular

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pressure decreases, heart dilatation ceases and the degree of resistance is overcome. That signifies, then, that ephedrin and adrenalin act on the insufficient conditions of the heart muscle fundamentally like digitalis and strophanthus glucoside; the difference lies in the promptness of the effect. The clinical results with adrenalin-ephedrin therapy in insufficiency of blood vessels is not so favorable as one would wish; hence true blood vessel insufficiency can hardly be remedied in human beings.

Disturbed Condition in Liver Therapy of Pernicious Anemia. — H. Taterka and Carl-Heinz Goldmann. (*Med. Klin.*, **25**: 1586, 1929.)

Only rather isolated reports (Ordway and Gorham, Davidson, McCrie and Gulland, Langstein) exist concerning secondary injuries with liver therapy. Four to 6 days after initiation of liver therapy in five cases of pernicious anemia, the author observed conditions of somnolence, extensive excitability and confusion. The clinical factor as a whole gave the impression of a dominant severe exacerbation. This condition lasted 2 to 3 days and then there was seen striking improvement of the general condition, with a very evident decrease of the anemia. The patient received liver up to a total daily amount corresponding to 1400 gm. of raw liver. The practical importance of the observation appears to the author to be the fact that an upset and collapsed condition occurs with the administration of particularly large amounts of liver, but this is not associated with any harm to the patient.

The Treatment of Ovarian Insufficiency with Sexual Hormone. — Harald Siebke. (*Münch. med. Wochenschr.*, **76** : 1752, 1929.)

All genital diseases which could likewise be improved with other remedies are unsuitable for the judgment of the success of hormone preparations. Along with the choice of cases, the choice of preparation to be administered plays a rôle. The sexual hormone has the best prospects and indeed, in the numerous clinical tests no harmful effect was ever observed when this hormone was used. The therapy with sexual hormone is not alone a substitution therapy, but often has a metabolic effect. The uterus once stimulated incites the ovary to increased activity by means of hyperemia of the pelvic layer, or the uterus, for example, in the treatment of amenorrhea, once initiated to menstruation after sexual hormone dosage, easily responds to the ovarian hormone stimulant in the future. Many times it is not necessary to continue the hormone treatment after one or two menstruations have been obtained. The therapeutic efficacy of the hormone preparation can be tested objectively in "growth tests" and in "tempo regulation tests." The growth test is positive if it is possible to make a small, underdeveloped incapable uterus, as the indication of vegetative ovarian insufficiency, a fully developed uterus which is capable of maintaining the monthly cycle and pregnancy; that signifies clinical improvement and cure of the symptoms evident through ovarian insufficiency.

The regulation tempo-test is positive if it is possible in amenorrhea, in cases of too seldom or too abundant bleeding as the sign of ovarian insufficiency, to induce a regular menstrual cycle, about every 4 weeks.

On the Significance of Endocrine Dermatoses in Woman. — M. Samuel and L. Strauss. (*Med. Klin.*, **25** : 1624, 1929.)

The prevalence of hyperglycemia is found in the climacterium, and if in young women, only in those with menorrhagias and painful disorders of menstruation due to ovarian dysfunction. It is relatively usual to observe an increase of blood sugar concentration during menstruation. This finding points, with apparent surety, to an endocrine relationship between the ovary and carbohydrate metabolism. In the majority of the authors' cases hyperglycemia was involved which was associated with the endocrine glands. These include such diseases as pruritus and intertriginous eczema. Insulin is recommended in these cases as well as in certain cases of menstrual disturbances (daily, 10 to 15 units of insulin for from several to 14 days) with relatively carbohydrate-poor diet.

Considerations and Facts of Endemic Thyroid Pathology. — W. Reyher. (*Würzburger Abhandl. Gesamtgeb. Med.*, New Series **6** : 179, 1929.)

The extraordinarily complicated pathology of endemic dystrophia with profound thyrogenous components, results alike in evidence of therapeutic success and of failure. In many cases it is possible to assuage the existing

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symptoms of insufficiency by means of thyroid gland therapy, as well as induce total subjective improvement. Objectively, however, one can determine the continuance of the vegetative and other components. The hypotonia, for example, remains unchanged. In other cases thyroid gland must be given with pituitary and sex glands in order to derive a reasonable result. In a large number of cases the therapy remains unsuccessful. In cases in which influenza preceded the thyropathia the author obtained important subjective improvement, that is, a totally healthy feeling, by the administration of thyroid gland tablets combined eventually with the administration of pituitary tablets and in all cases combined with Ca Ph (phytophosin). In individual cases, at any rate, recovery of the thyroid seems to ensue by means of the substitution therapy, even when it must seem to the physician that a relapse is imminent.

On the Polarization Capacity of Skin in Psychoses and Its Relation to the Function of the Thyroid Gland. — Ch. Roggenbau and W. Lueg. (*Monatsschr. Psychiat. u. Neurol.*, **78** : 301, 1929.)

From their investigations the authors draw the conclusion that in the disease picture of manic depressive irrationality, in contrast to schizophrenia, as a rule, thyroid gland disturbances play no insignificant rôle, and that a series of body symptoms, especially circulatory and metabolic disorders, which are to be seen in manic depressives, are dependent upon them.

On the Chemistry of the Pituitary Anterior Lobe — Sexual Hormone. — M. Reiss and F. Haurowitz. (*Zeitschr. ges. exp. Med.*, **68** : 371, 1929.)

The water-soluble preparations derived from the anterior lobe of the pituitary were disintegrated with weak concentrations of acids, with strong lye, with temperatures over 70° and also with oxidation mediums, for example, with 1 per cent H_2O_2. The raw preparation derived from the urine contains in addition to organic salts the amino-acids of the urine and "urine peptides." The author has accomplished the feat of binding this active substance to aluminium hydroxide or to the precipitation derived by means of uranylacetate, and thus to obtain a purification of three or four times. With regard to the control of the enzyme it is to be assumed that the hormone stands closer to the peptone than to the dipeptide. It is understood that the hormone is in large part inactivated by peroral administration. In order to derive the same effect as with parenteral dosage the oral dose must be increased 150 times. The hormone extracted from the gland in many ways resembles the substance from the urine. It is soluble in water and is obtained from this solution with alcohol and also is attacked in a similar manner by the proteolytic enzyme as the substance derived from the urine. From these investigations it must be concluded that the product derived from the urine is closely related to that of the anterior lobe of the pituitary.

Menstrual Dermatoses. — S. Recausens. (*Med. Welt*, **3** : 1497, 1929.)

Everything relating to the treatment of dermatoses during menstruation is still doubtful, and the results obtained in many cases of ovarian and pituitary insufficiency are very uncertain. The therapy with preparations from the ovary and its various components is to be preferred above all others. Unfortunately results have not been obtained in the beginning which would lend encouragement. Ovarian extract, corpus luteum extract, the hormone folliculin, "Tyro-Ovarin-ovarian pituitary hormone" have not caused the desired activity of the ovary in the majority of cases and have made possible the institution of increase of menstrual bleeding. Roentgen ray stimulation treatment of the ovary and pituitary in instances of insufficiency of these glands, must be tested, likewise transplantation of ovary may induce good results.

On the Influence of Thymus and Spleen Extracts on Calcium Metabolism. — M. Reiss, K. Winter and N. Halpern. (*Endokrinologie*, **5** : 230, 1929.)

On the basis of their experiments the authors come to the conclusion that: In short experimental tests, thymus extracts act invariably to decrease blood calcium content. Thymus extracts injected in longer processes, effect an increase of total calcium and a calcium enrichment of the bones. Spleen extracts act in the same way as thymus extracts. Extracts of muscle and liver are ineffective.

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Investigations on the Inhibition of Post-Operative Thrombosis and Embolism by Means of Ingestion of Thyroxin. —H. L. Popper. (*Med. Klin.*, **25**: 1588, 1929.)

In 150 cases treated with synthetic thyroxin, there were found a mortal lung embolism and three instances of thrombophlebitis with one lung infarct; 150 untreated cases exhibited post-operatively 4 instances of thrombophlebitis, no lung infarcts, no embolism. Synthetic thyroxin exhibits no harmful secondary effects in any case. Of 50 cases treated with natural thyroxin 2 cases of thrombophlebitis were found of which one was a non-fatal lung embolism; in the 50 control cases, 1 mortal lung embolism and 1 thrombophlebitis. After natural thyroxin in the amount of 3 mg. per day in several cases there resulted symptoms of thyroidism. Because a prophylactic effect of thyroxin ingestion with regard to the occurrence of thrombophlebitis and lung embolism is not observed in the experimental investigations of the author, he maintains that the administration of thyroxin for this purpose is not indicated.

Concerning the Administration of Hypophysin in Nephrolithiasis. — H. Naumann. (*Med. Klin.*, **25** : 1623, 1929.)

A report on the experiences with 50 patients. An effect with hypophysin is only to be expected if the calculus has already entered the ureter; the smooth musculature here, more abundant than in the pelvis of the kidney, reacts more promptly to hypophysin. The number of instances of elimination of calculi with hypophysin (three times in 50 cases) does not surpass the percentage of these cases in which spontaneous stone elimination occurred without artificial aid. The hypophysin method in differential diagnosis often fails, as one may expect from the theoretical considerations.

Concerning the Adrenalin Effect on Isolated Guinea Pig Uterus, Dissociated from Cycle Hormone. — M. Kochmann and H. Seel. (*Zeitschr. ges. exp. Med.*, **68** : 238, 1929.)

The uterus of the guinea pig gives evidence of various spontaneous forms of movement, and especially various reactions to adrenalin, according to the hormonal condition in which the animal is found. During estrus contraction always follows adrenalin application, that is 1 day previous and 4 days after. In non-castrated guinea pigs the adrenalin inhibition appears to be strongest in the interestrum.

Criticism of the Pharmacological Therapy of the Digestive Tract. — Paul Trendelenburg. (*Med. Klin.*, **25** : 1800, 1929.)

The inhibition of the intestinal vago-stimulus was made possible by means of adrenalin, but the effect of adrenalin in peroral dosage chiefly has a local influence on the mucous membrane. An increased sensitization of the intestinal musculature itself is best accomplished by the extract of the posterior lobe of the pituitary which affects the ileum and colon.

Experimental Researches on the Influence of Extracts of the Anterior Lobe of the Pituitary on the Genital Apparatus of Rabbits and on Milk Production. — P. Stricker and F. Grueter. (*Deut. med. Wochenschr.*, **55** : 1942, 1929.)

In rabbits in which ovulation had been induced, extracts of the anterior lobe of the pituitary led to rupture of the mature follicle and formation of corpora lutea which induced an effect on the uterus typical of that resulting from coitus. Extract of the anterior lobe of the pituitary exercises a noteworthy effect on milk secretion even after elimination of the ovaries (castration) so that the mammary glands are primarily prepared by the corpus luteum. On the other hand, it is easy to call forth these secretory indications again in animals (rabbits, female dogs) which have already delivered their young and no longer secrete milk. Finally, it is possible in castrated rabbits, even several months after castration and several weeks after total cessation of lactation, to obtain a reinstitution of milk secretion in quite small, retrogressed mammary glands.

The Experimental Basis of the Theory concerning the Mechanism of Action of Liver Diet Therapy. — Karl Singer. (*Wien. klin. Wochenschr.*, **42** : 1593, 1929.)

The experimental analysis of the mechanism of action of liver diet therapy has shown that in the symptom complex two factors must be differentiated. 1. A new blood formation and a blood decomposition-promoting impetus of non-specific sort, which is the property of liver as well as of flesh, but not of

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liver extract. 2. A specific principle which is also contained in liver extract and which is required for the production of valid red blood corpuscles in uninvolved perniciosa.

It is further demonstrated that the quantitative method of administration up to the present is not sufficient alone for the explanation of many problems of normal and pathological blood conditions, that more often the quality of the erythrocyte production must be considered. The biophysical and biochemical construction of red blood corpuscles is, however, an entirely unexplored realm. For the acquisition of knowledge, there is here, as usual, the urgent need of functional hematology.

Concerning Individual Effects of Parathyroid Preparations. — Anna Sucher. (*Wien. klin. Wochenschr.*, **42** : 1504, 1929.)

In a 62 year old woman suffering from painful condition of the bones, angio-neurotic edema, general debility and mental depression, prompt relief through parathyrin was obtained and also elimination of these symptoms. Not only parenteral, but oral dosage, too, was accompanied by the same success, a circumstance which is significant on account of the duration of treatment.

The Possibilities and Limitations of Liver Therapy. — R. Seyderhelm. (*Deut. med. Wochenschr.*, **54** : 1704, 1929.)

According to the present state of affairs as recorded in the literature, in most cases anemia is warded off as long as liver is administered. The singular fatal cases are explained as due to inadequate amounts of liver, calcium complications, toxic injuries of the central nervous system, intercurrent diseases (sepsis, pyelitis, pneumonia). The problem of dosage is very important, particularly at the commencement of treatment of very severe cases. At most 200 to 500 gm. of liver is required. Often by means of a "liver deluge" (up to 1200 gm. daily) in apparently refractory cases, too, an alteration in tone may be obtained. In such amounts the combination of peroral and rectal administration is recommended. The disappearance of urobilin and urobilinogen from the urine, the appearance of reticulocytes and the accumulation of hemoglobin and erythrocytes serve as first criteria for the effect, at the same time as control for the amplitude of the dosage. A sudden release of normoblasts with decrease of hemoglobin and erythrocyte values is the "desperate crisis of the bone marrow" suggesting a suspicion of carcinoma metastases in the bone marrow. The toxic symptom in the central nervous system, funicular myelitis, remains uninfluenced by liver therapy (few reports to the contrary). Hence, the disease picture is quite a new sort. After dropping off of the anemia the pernicious anemia is changed into a pernicious myeloencephalotoxicosis (hallucinations, severe disturbances of speech, coma with Kussmaul type of respiration). Hence liver therapy is not a causal, but rather a symptomatic therapy, directed against an established symptom complex.

Concerning the Action of Kidney Extracts on Functional Conditions of Kidney Contraction. — K. Stejskal. (*Med. Klin.*, **1** : 1015, 1929.)

After intracutaneous injection of 2 to 5 cc. of a watery kidney extract or a lipoid-containing extract, albumin-free, however, of this organ, a definite drop in blood pressure was observed in several patients with primary or secondary contracted kidney. The effect on the blood pressure is organ specific, that is it follows only after injection of kidney extracts (not after extracts of liver or brain) and only in nephritic hypertonics. The indication of an effect not only of albumin substances but also of lipoid extracts of the kidney on blood pressure has a practical as well as a theoretical significance. The fall in blood pressure can be spoken of as a direct effect of administration of the extract or as a secondary effect as a result of local vasodilatation of the kidney and hence associated improvement of the blood supply of the kidney. Perhaps there is a relation between the substances contained in the kidney extract and the Frey circulation hormone from the urine.

Book Reviews

"Rembrandt." By J. G. De Lint. Monograph Series of Great Painters and Their Works As Seen by a Doctor, Published by J. Philip Kruseman, The Hague, Holland. No. 1, 113 pages, cloth, $2.50.

This book contains a large number of reproductions of the paintings, etchings and

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drawings of the greatest of all Dutch painters — Rembrandt — of subjects relating to medicine and physicians. Some of the drawings are of the greatest interest to the physician as indications of Rembrandt's unequalled ability to preserve with a few lines his impressions and observations of subjects, doubtless material for future use in his finished works. His portrayal of the face in pain, emotion, sleep, and fatigue and the postural accompaniments of these states give evidence of his peculiarly well developed power of observation. Apparently the great artist's eye caught details perhaps overlooked by the physician whose thoughts were occupied not only with observing facts but in attempting to relate them to some of the involved theories of medicine of the time. (Perhaps too warm an attachment for a theory may have created a "mental hazard" in observing some facts on the part of the physician.) In the painting "The Lecture on Anatomy of Nicolaas Tulp" Rembrandt has portrayed the tendons of the flexor profundus digitorum perforating those of the more superficial flexor sublimis digitorum showing the insertions of each which make possible the flexing of the several phalanges. Extraordinary observations must have been supplemented by the advice of the anatomist himself in this case.

The textual matter gives one the feeling of familiarity with both the picture and with Rembrandt.

Pictures and discussions from medical subjects of the Bible and from every day life receive about equal treatment. To the physician who is a lover of painting the book is of extraordinary interest. To the physician who has not been greatly interested in art it will likely stimulate such an interest, for the subject matter is peculiarly the physician's own.

"Medical Art Calendar." Published by J. Philip Kruseman, The Hague, Holland, 1930.

This is the 1930 edition of the "Medical Art Calendar."

Each page contains a splendid reproduction of a work of one of the old Masters dealing with medicine. The description is in both Dutch and English. There are one reproduction and two weeks' dates to a page, and blank spaces for memoranda. It is a very artistic production and would grace any physician's office.

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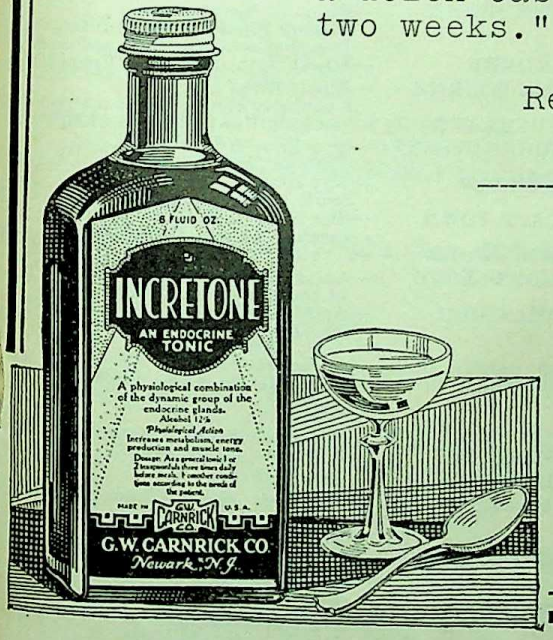
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One Physician's Experience with Incretone

"I want to thank you for the samples you sent me of your tonic. I'm giving it to my wife, and I think she is improving nicely. She has been in wretched health for 15 years. She has been improving ever since I put her on the tonic. I want to say that I have prescribed it in a dozen cases in the past two weeks."

Respectfully,

_____M.D.



G. W. Carnrick Co.

Dependable Gland Products

20 Mt. Pleasant Ave. Newark, N. J.

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AMENORRHEA

is almost entirely an endocrine disease

"There is no doubt that menstruation depends on the functional activity of the ovary."
(*Human Physiology*---Starling)

More recently the indispensable part played by the anterior pituitary has been demonstrated. The primary action of the two hormones of the anterior pituitary on the graafian follicle and corpus luteum is one of the most convincing examples of endocrine interrelationship ever given.

HORMOTONE

makes these active, potent anterior pituitary and ovarian hormones available for every day use



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G. W. Carnrick Co.
Dependable Gland Products
20 Mt. Pleasant Avenue
NEWARK, N. J.

For General Information and Literature Address
G. W. CARNRICK CO.
20 Mt. Pleasant Ave., Newark, N. J., or
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Contractor House, Nicol Road,
Ballard Estate, Bombay

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Single Gland Products

OUR organotherapeutic products are made from fresh glands of healthy food animals, in our own laboratory, under the supervision of competent chemists. All moisture has been removed from these gland products and they will keep indefinitely if contents are not exposed to moisture and bottle is kept tightly corked.

The manufacture of gland extracts is not a side line with us, but is our only specialty, our only business. We stand or fall on their quality and potency.

We can furnish prices on 1/4 lb., 1/2 lb. and 1 lb. lots of Single Gland Powder.

Amylzyme (High Test Pancreatin) — Powder, 1 oz.; Caps., 40, 100.

Brain Sub. — Powder, 1 oz.

Brain and Spinal — Tabs., 2-gr., 100, 500, 1000.

Corpus Luteum — Powder, 1/8 oz., 1 oz.; Chocolate Coated Tabs., 2-gr., 50, 100, 500, 1000; Tabs., 5-gr., 50, 100; Caps., 5-gr., 50, 100; 1-cc. Amps., 1/2 doz.

Duodenal Sub. — Powder, 1 oz.

Epinephrine, Powder, 1 gr.

Epinephrine Chloride Solution — (1:1000), 1 oz.

Epinephrine Chloride Solution, (1:10,000) 1-cc. Amps., 1/2 doz.

Kidney Sub. — Powder, 1 oz.; Tabs., 2-gr., 100, 500, 1000; Caps., 5-gr., 100.

Lecithin — Jar, 1 oz.

Liver Sub. — Powder, 1 oz.; Tabs., 3-gr., 100, 500, 1000; Caps., 5-gr., 100.

Mammary Sub. — Powder, 1 oz.; Tabs., 1-gr., 100; Tabs., 3-gr., 100, 500, 1000; Caps., 5-gr., 100.

Marrow, Red Bone, Glyc. Ext. — 1/2 pt., 1 pt.

Orchic Sub. — Powder, 1 oz., Chocolate Coated Tabs., 2-gr., 100, 500, 1000; Caps., 5-gr., 100.

Ovarian Sub. — Powder, 1 oz., Tabs., 1-gr., 100; Chocolate Coated Tabs., 2-gr., 100, 500, 1000; Tabs., 5-gr., 50, 100, 500, 1000; Caps., 5-gr., 50, 100.

Ovary without Corpus Luteum — Powder, 1 oz.; Caps., 5-gr., 100.

Pancreas Sub. — Powder, 1 oz.; Tabs., 2-gr., 100, 500, 1000; Caps., 5-gr., 100.

Pancreatin (U. S. P.) — Powder, 1 oz.

Pancreatin and Soda — Tabs., 100, 500, 1000.

Parathyroid Sub. — Powder, 1/8 oz.; Tabs., 1/20-gr., 100, 500, 1000; Tabs., 1/10-gr., 100.

Pepsin (U. S. P.) — Powder, 1 oz.

Pineal Gland Sub. — Powder, 1/8 oz.; Tabs., 1/10-gr., 100, 500, 1000.

Pituitary, Entire — Powder, 1/8 oz., 1 oz.; Tabs., 1/2-gr., 50, 100, 500, 1000; Tabs., 1-gr., 50, 100, 500, 1000; Tabs., 2-gr., 50, 100, 500, 1000.

Pituitary, Anterior — Powder, 1/8 oz., 1 oz.; Tabs., 1-gr., 50, 100, 500, 1000; Tabs., 2-gr., 50, 100, 500, 1000.

Pituitary Posterior (U. S. P.) — Powder, 1/8 oz.; Tabs., 1/10-gr., 100, 500, 1000; Tabs., 1/2-gr., 100, 500, 1000.

Post Pituitary Solution (Liquor Pituitarii) Obs. — 1/2-cc. Amps., 1/2 doz.; 1-cc. Amps., 1/2 doz.

Placenta Sub. — Powder, 1 oz.; Chocolate Coated Tabs., 3-gr., 100, 500, 1000; Caps., 5-gr., 50, 100.

Prostate Sub. — Powder, 1 oz.; Chocolate Coated Tabs., 2-gr., 100, 500, 1000; Caps., 3-gr., 100.

Spleen Sub. — Powder, 1 oz.; Tabs., 3-gr., 100, 500, 1000; Caps., 5-gr., 100.

Suprarenal (See also Epinephrine) — Powder, 1 oz.; Tabs., 1-gr., 100, 500, 1000; Caps., 3-gr., 100.

Suprarenal Cortex — Powder, 1/8 oz., 1 oz.; Tabs., 1-gr., 50, 100, 500, 1000; Tabs., 2-gr., 50, 100; Caps., 3-gr., 50.

Suprarenal Medulla — Powder, 1 oz.; Tabs., 2-gr., 100.

Thymus Sub. — Powder, 1 oz.; Tabs., 3-gr., 100, 500, 1000; Caps., 5-gr., 100.

Thyroid (U. S. P.) — Powder, 1 oz.; Tabs., 1/100-gr., 100; Tabs., 1/10-gr., 100, 500, 1000; Tabs., 1/4-gr., 100, 500, 1000; Tabs., 1/2-gr., 100, 500, 1000; Tabs., 1-gr., 100, 500, 1000; Chocolate Coated Tabs., 2-gr., 100, 500, 1000; Caps., 1-gr., 100; Caps., 2-gr., 100; Caps., 3-gr., 100; Caps., 5-gr., 100.

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Specialties

HORMOTONE

Neurasthenia; "run-down conditions"; suboxidation; neuroses; menstrual and climacteric disorders; cardiac asthenia; hypotension, etc.

A combination of tonic hormones from thyroid, pituitary, suprarenal and gonads.

Dose: 1 or 2 tablets 3 times daily before meals.

Tablets: 50 and 100.

TRYPSOGEN

Diabetes mellitus; glycosuria and defective carbohydrate metabolism. Also useful in certain pancreatic disorders, and as an adjunct in hypertension.

Presents the homostimulative principles that excite the production of the internal secretion of the pancreas when the gland is functionally deficient; proteolytic and lipolytic ferments, 1/200 gr. each of gold bromide and arsenic bromide.

Dose: 5 to 7 tablets or capsules after meals.

Tablets 100, 500, 1000; Capsules 100; Capsules Double Strength 100.

TRYPSOGEN—ENTEROSOL COATED

Trypsogen may now be obtained in enteric coated tablets which pass through the stomach unchanged and dissolve in the intestine, ready for immediate absorption. Same sizes as Trypsogen.

MAMMAGEN

To increase lactation in deficient milk supply in the nursing mother.

Each tablet contains 1/8 grain desiccated entire pituitary substance with the hormones and vitamines of corpus luteum, placenta and mammary glands.

Dose: 1 or 2 tablets or capsules three times daily after meals.

Tablets 50, 100; Capsules 50.

ERYTHGEN LIVER EXTRACT

Erythgen Liver Extract is a highly potent derivative of the liver containing the hematopoietic principles useful in the treatment of anemia. It is a brown powder, completely soluble in water and practically protein free. One part of the powder represents approximately 40 parts of fresh liver substance.

The activity is controlled by graphs showing the time of recovery of experimental anemia in animals following absorption of the powder from the stomach.

Supplied in 8 oz. bottles of solution in glycerin.

Dose: From 1 to 4 teaspoonfuls, t. i. d. May be increased if necessary.

VIRILIGEN

Indicated in lowered virility and sexual neurasthenia of functional origin.

Presents desiccated extracts of anterior pituitary suprarenal cortex, lymph, brain and spinal cord substance, testis and 1/10 gr. thyroid. Not sold in bulk.

Dose: 1 or 2 tablets or capsules three times daily before meals.

Tablets 100; Capsules 100; Ampoules 1/2 doz.

SECRETOGEN

A physiological treatment of gastrointestinal insufficiencies and constipation, intestinal stasis, infantile diarrheas, marasmus and inanition.

Tablets: A homostimulative extract from the duodenum.

Dose: 1 to 3 tablets before or after meals.

Tablets 100, 500, 1000.

Elixir: A homostimulative extract from the stomach and duodenum; contains 1/10 of 1% HCl.

Dose: 1 to 3 teaspoonfuls before or after meals.

Elixir 1/2 pt., 1 pt., 5 pts., 1 gal.

KINAZYME

An aid to metabolism in tuberculosis and other wasting diseases; especially valuable in undernourished and backward children.

Each tablet contains 1/60 gr. pituitary entire, 1/40 gr. parathyroid, in addition to pancreas, liver and spleen substance with calcium phosphate.

Dose: 2 to 4 tablets or capsules after eating.

Tablets 100, 500, 1000; Capsules 100.

INCRETONE

A liquid endocrine tonic. Incretone is a general tonic for use in all cases in which general tonic treatment is indicated. It combines the advantages of an effective bitter tonic with the definite stimulus to metabolism of endocrine therapy.

Each teaspoonful contains the soluble and active constituents of 1/10 gr. thyroid, 1/60 gr. entire pituitary, 1/10 gr. ovarian and 1/10 gr. orchic substance.

Dose: For adults, one or two teaspoonfuls before meals. Children in proportion.

Bottles of 6 ozs.

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Treat the Diabetic Patient



So much stress has been placed on the treatment of the disease that the patient has been largely forgotten. Increase the patient's strength by adjusting and restricting the diet and give

TRYPSOGEN

an effective pancreas product for oral administration.

Aids in the utilization of sugar
Aids in the storage of glycogen in the liver
Increases the strength of the patient

Trypsogen: Bottles of 100, 500 and 1000 tablets.
Trypsogen---Enterosol Coated: Bottles of 100, 500 and 1000 tablets

G. W. CARNRICK CO.

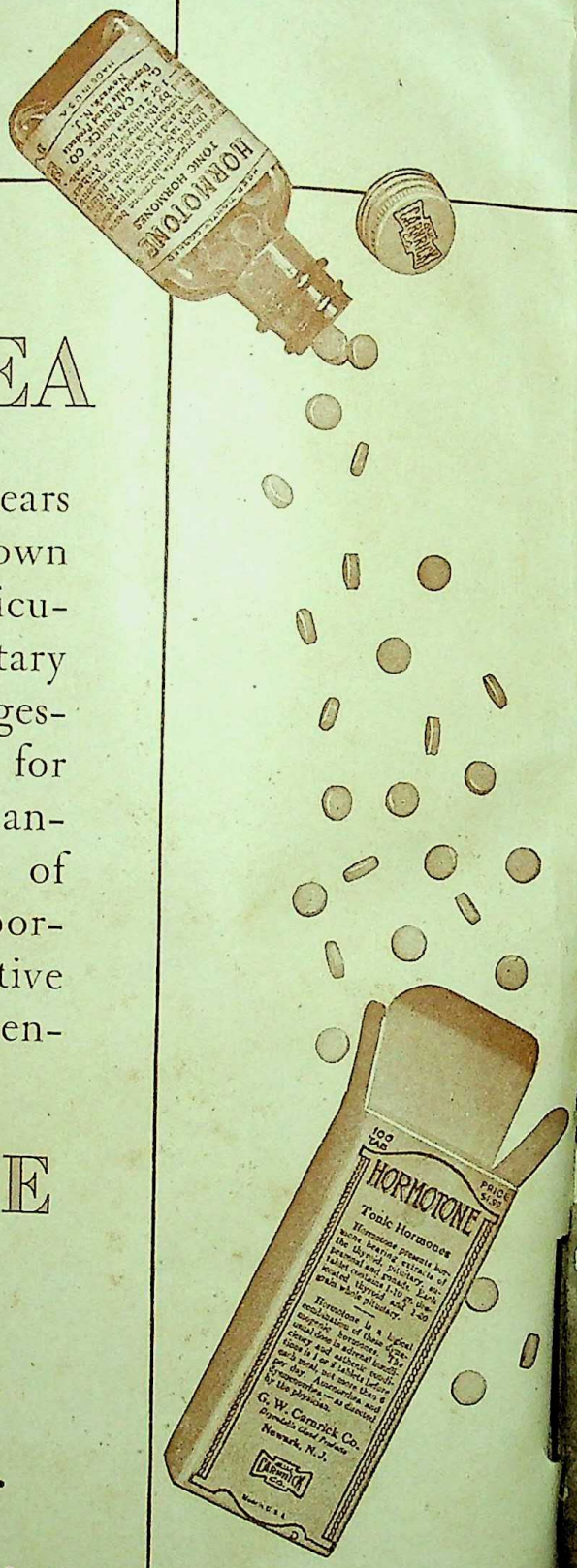
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AMENORRHEA

Research of the past few years has shown that the two known hormones of the ovary, follicular and luteal, are supplementary in initiating the uterine progestational changes necessary for normal menstruation. The anterior pituitary, the "motor of the ovary," is of equal importance. For a potent effective combination of these indispensable elements prescribe

HORMOTONE

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